

Pharvaris N.V.
Annual Report
for the fiscal year ended December 31, 2023

[1 Table of Contents](#)

Pharvaris N.V. TABLE OF CONTENTS

	<u>Page</u>
Report of Board of Directors	
1 Introduction	2
1.1 Preparation	2
1.2 Forward-looking statements	2
2 Business	4
2.1 History and development of the company	4
2.2 Overview	4
2.3 Organizational structure	36
2.4 Property, plants and equipment	36
2.5 Operating results	36
2.6 Material subsequent events	44
3 Risk factors	45
3.1 Summary of key risk factors	45
3.2 Risk factors	46
4 Controls and procedures	81
4.1 Risk management and control systems	81
4.2 In control statement	83
5 Corporate Governance	83
5.1 Dutch Corporate Governance Code	83
5.2 Code of business conduct and ethics and other corporate governance practices	84
5.3 Risk management and control systems	81
5.4 General Meeting	84
5.4.1 Functioning of the General Meeting	84
5.4.2 Powers of the General Meeting	85
5.4.3 Shareholder rights	85
5.5 Board	85
5.6 Committees	87
5.6.1 General	87
5.6.2 Audit committee	87
5.6.3 Compensation committee	89
5.6.4 Nomination and corporate governance committee	89
5.7 Evaluation	90
5.8 Diversity	90
5.9 Corporate values and code of business conduct and ethics	91
6 Compensation	91
6.1 Compensation policy	91
6.2 Compensation of directors	92
6.3 Pay ratio	92
7 Related party transactions	92
8 Protective Measures	92
9 Financial Statements	
Consolidated Financial Statements	
10 Company Financial Statements	
Company only Financial Statements	
Other information	
Independent auditor's report	
Profit appropriation provisions	
Shares carrying limited economic entitlement	
Branches	

[2 Table of Contents](#)

1. Introduction

1.1 Preparation

In this report, the terms "we", "us", "our" and "the Company" refer to Pharvaris N.V. and, where appropriate, its subsidiaries.

This report has been prepared by the Company's board (the "**Board**") pursuant to Section 2:391 of the Dutch Civil Code ("**DCC**") and also contains (i) the Company's statutory annual accounts within the meaning of Section 2:361(1) DCC and (ii) to the extent applicable, the information to be added pursuant to Section 2:392 DCC. The 2023 consolidated financial statements are prepared in accordance with the IFRS as issued by the European Union (IFRS-EU) and the company financial statements including the notes thereon have been prepared in accordance with Part 9 of Book 2 of the Dutch Civil Code. Section 2:362 (8) of the Dutch Civil Code, which allows companies that apply IFRS-EU in their consolidated financial statements to use the same measurement principles in their company financial statements. This report relates to the fiscal year ended December 31, 2023 and, unless explicitly stated otherwise, information presented in this report is as at December 31, 2023.

1.2 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 PHVS416 (immediate-release deucricitbant capsules) and PHVS719 (extended-release deucricitbant 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, such as the COVID-19 pandemic, 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 PHVS416 and PHVS719 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 PHVS416 and PHVS719 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;

3 Table of Contents

- 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 successfully remediate the material weaknesses in our internal control over financial reporting and to maintain an effective system of internal control over financial reporting;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act or a foreign private issuer; and
- changes and uncertainty in general market, political and economic conditions, including as a result of inflation and the current 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.

[4 Table of Contents](#)

2. Business

2.1 History and development of the Company

We are a clinical-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, deucricitbant (PHA121, PHA-022121), is a novel, small-molecule bradykinin-B2-receptor antagonist for the treatment of hereditary angioedema, or HAE. Bradykinin-B2-receptor inhibition is a clinically validated mechanism for the treatment of HAE, as demonstrated by icatibant, which is a bradykinin-B2-receptor antagonist approved in Europe in 2008 and in the United States in 2011 (as FIRAZYR). PHA121 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 deucricitbant to improve upon the therapeutic profile of existing therapies and, through oral delivery, to provide patients with quality of life and ease-of-administration that is superior to current standard-of-care HAE treatments, which are injectables. We believe deucricitbant has the potential to provide a safe, effective and easy-to-administer option for both acute and prophylactic treatments of HAE, in the form of our PHVS416 (deucricitbant immediate-release (IR)) on-demand rapid exposure product candidate, and for prophylaxis of HAE, in the form of our PHVS719 (deucricitbant extended-release (ER)) small daily dose extended-release product candidate. We believe that our product candidates may address a broader range of angioedema attacks than other available treatments since deucricitbant blocks the actual signal that leads to angioedema (the interaction of bradykinin, or BK with the bradykinin-B2-receptor), rather than an upstream signal. By blocking the action of bradykinin, we can prevent its aberrant signaling regardless of the pathway that generates it.

In our completed Phase 1 trials to date, we have observed that deucricitbant was orally bioavailable and well tolerated at all doses studied, with approximately dose-proportional exposure. We also have successfully demonstrated proof-of-concept through a clinical pharmacodynamics, or PD assessment with the bradykinin challenge, which had been utilized as a validated surrogate assessment for dose selection in the icatibant development program.

We have demonstrated clinical efficacy and tolerability in a Phase 2 study (RAPIDe-1) treating attacks of HAE. The data allowed us to compare the projected therapeutic performance of deucricitbant with that of icatibant. However, we have not conducted a head-to-head comparison of icatibant to deucricitbant in a clinical study. We plan to efficiently progress deucricitbant through clinical development for on-demand and prophylactic use with our on-demand immediate-release product candidate, PHVS416, and prophylactic extended-release product candidate, PHVS719, respectively. We commenced our RAPIDe-1 Phase 2 clinical trial of PHVS416 in February 2021 and reported topline Phase 2 data for the acute treatment of patients with HAE attacks in December 2022. We have also demonstrated clinical efficacy and tolerability in a Phase 2 study (CHAPTER-1) for prophylaxis of HAE attacks. We commenced the CHAPTER-1 Phase 2 clinical trial for prophylaxis in 2021 using twice-daily dosing of the PHVS416 soft capsules and announced positive topline data in December 2023. Our primary objective with this trial was to assess the efficacy and safety profile of PHVS416 dose regimens for prophylactic treatments in HAE patients. In February 2022, we reported Phase 1 clinical data with PHVS719 demonstrating pharmacokinetics of the extended-release formulation and the potential for once-daily dosing. In healthy volunteers, a single dose of PHVS719 was well tolerated with an extended-release profile supporting once-daily dosing.

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 founded in 2015 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 Dr. Morgan Conn, who is registered in PO Box 121, Buckingham PA 18912, 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.

2.2 Overview

Deucricitbant (PHA121, PHA-022121) is a novel, highly potent inhibitor and selective small molecule bradykinin-B2-receptor antagonist and, to our knowledge, the only orally available bradykinin-B2-receptor antagonist currently in development. Deucricitbant 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. PHA121 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 deucricitbant as a new chemotype with properties compatible with oral delivery. We are developing deucricitbant for the on-demand indication as PHVS416, which is delivered in a softgel capsule designed to rapidly treat symptoms with a single dose. We are also developing deucricitbant for the prophylactic indication as PHVS719, which is a small daily dose tablet with an extended-release formulation designed for the patient to

[5 Table of Contents](#)

maintain therapeutic levels for at least 24 hours and to achieve a steady-state plasma concentration within 72 hours. We have released topline data from our RAPIDe-1 study demonstrating efficacy and tolerability in our Phase 2 clinical trial for treatment of HAE attacks on demand using PHVS416 and topline data from our CHAPTER-1 study demonstrating efficacy and tolerability of deucricitbant for the prophylactic treatment of HAE attacks. CHAPTER-1 used twice daily dosing of PHVS416 for proof-of-concept. We intend to use PHVS719 extended-release deucricitbant in further trials and commercially for prophylaxis.

In our Phase 1 clinical trials to-date, we have observed rapid exposure and predictable linear pharmacokinetics, or PK, with and without food. In addition, we observed deucricitbant to be a potent antagonist of the bradykinin-B2-receptor, in vitro and in vivo with healthy volunteers. In our models based on PK data from our Phase 1 clinical trial of deucricitbant and published data for icatibant, both in the BK challenge assessment, deucricitbant was shown to be consistently 25-fold more potent at inhibiting the effects of administered bradykinin than icatibant on a molar basis. We have not conducted a head-to-head comparison of icatibant to deucricitbant in a clinical trial but have compared the published data for icatibant to data from our Phase 1 and Phase 2 clinical trials of deucricitbant. 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.

In our Phase 2 placebo-controlled trial evaluating the efficacy and tolerability of PHVS416 for on-demand treatment of attacks in patients with HAE type 1 and 2 (RAPIDe-1), a statistically significant and clinically meaningful reduction of the patient-reported symptoms of HAE was observed for the attacks treated with all doses of PHVS416 (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, PHVS416 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, PHVS416 substantially reduced the use of rescue medication compared to the placebo. PHVS416 was generally well tolerated at all dose levels with three treatment-related adverse events (TRAEs) reported for one PHVS416 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 believe these positive Phase 2 data support further development of PHVS416 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 deucricitbant for long-term prophylaxis against angioedema attacks in HAE type 1 and 2 (CHAPTER-1), a statistically significant and clinically 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 deucricitbant significantly reduced the mean monthly HAE attack rate by 84.5% compared to placebo.

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 1:50,000 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.

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. 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.

Based on results observed from our four completed clinical trials to-date, we believe our product candidates that contain deucricitbant will demonstrate advantages and differentiation relative to currently approved HAE therapies and other oral therapies in clinical development. Deucricitbant's bradykinin-B2-receptor-inhibition mechanism has a well-established clinical therapeutic profile in a currently approved product in the rapid treatment of acute HAE attacks. We have observed greater potency for deucricitbant compared to icatibant using a surrogate endpoint in the bradykinin challenge study, potentially resulting in both a smaller therapeutic dose and a longer duration of effect. We evaluated the PD and PK of deucricitbant in a bradykinin-challenge model in healthy subjects. 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. We conducted a proof-of-concept clinical trial testing the effects of BK in healthy volunteers in our bradykinin-challenge trial, where we evaluated the effect of deucricitbant on cardiovascular parameters affected by bradykinin such as blood pressure, heart rate and cardiac output in healthy volunteers. We observed that deucricitbant was more potent in blocking the effects of BK in humans than icatibant, when comparing the deucricitbant results of the trial to published data on icatibant. The data from this trial allowed us to generate a PK/PD correlation model. Based on this model and published data on icatibant, we predict the duration of effect for a single oral dose of 12 mg deucricitbant to exceed that of 30 mg of icatibant and a single oral

6 Table of Contents

dose of 22 mg deucricitbant will cover the same duration of effect as two icatibant injections of 30 mg administered six hours apart. Furthermore, analysis based on the results from this trial suggest that therapeutic doses of deucricitbant may be at least 10-fold smaller than the doses required for oral kallikrein inhibitors in development. In addition, we believe that the observed PK profile of our compound demonstrates the potential of PHVS719 as a prophylactic treatment of HAE by achieving steady-state plasma concentrations within 72 hours. The BK-challenge data was generated in a Phase 1 clinical trial. The topline data from our deucricitbant Phase 2 RAPIDe-1 trial treating HAE attacks were consistent with the predictions of the BK challenge in both onset of symptom relief and duration of effect (use of rescue medication). However, we have not conducted a head-to-head comparison of icatibant to deucricitbant in a clinical trial but have compared the published data for icatibant to data from our Phase 1 clinical trial of deucricitbant. 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.

In August 2022, the FDA placed a hold on the clinical trials of deucricitbant 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 deucricitbant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucricitbant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study.

Additional trials may be required by the FDA, EMA or other regulators even with positive data from RAPIDe-1 and CHAPTER-1. We are also planning to conduct a registration-directed trial in the on-demand setting and a registration-directed trial with patients who will be randomized to receive PHVS719 or placebo to assess safety and efficacy in HAE patients. In addition, we also plan to run an open-label extension study in the prophylactic setting with both rollover and non-rollover subjects to collect longer duration safety data.

Differentiation of deucricitbant

We believe that deucricitbant, as the molecule underlying both PHVS416 and PHVS719, has the potential to be highly differentiated for both the on-demand and prophylactic settings with the key benefits below:

PHVS416. We believe that PHVS416, 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 (EC85) in 30 minutes, with or without food

Potential Reduced Treatment Burden / Enhanced

- No injection needed

Patient Convenience

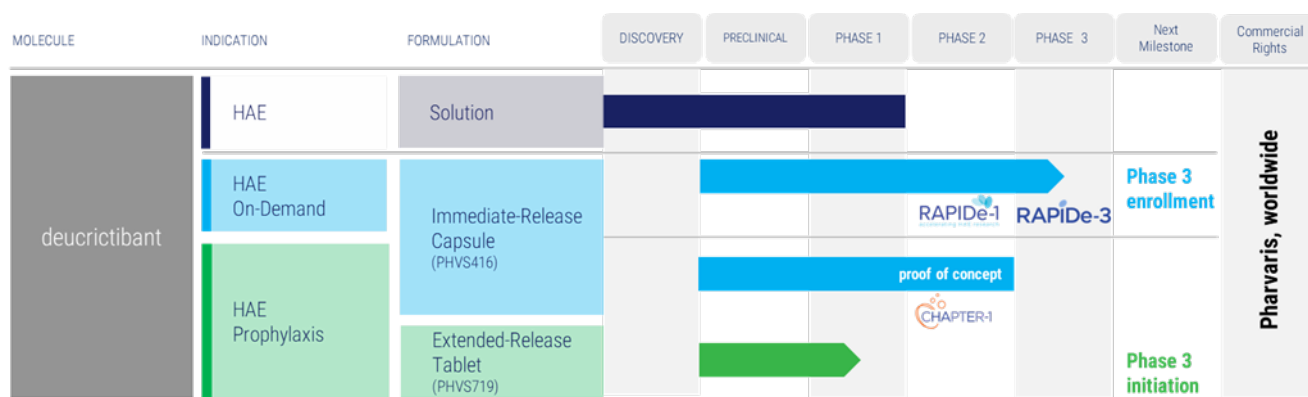
- Convenient oral formulation removes barriers inherent in current injectable treatments to facilitate early treatment of acute HAE attacks and overall treatment of more attacks than currently reported
- Capsule reduces treatment burden
- Potential lowest dosage of any oral HAE on-demand treatment

7 Table of Contents

PHVS719. We believe that PHVS719, a prophylactic extended-release tablet designed to be taken in small, daily doses, has the potential to be highly differentiated for HAE patients with the following benefits:

Protection From Attacks	<ul style="list-style-type: none"> Validated, proven mechanism to address all bradykinin, regardless of pathway
Ideal Release Profile for Prophylactic Use	<ul style="list-style-type: none"> Reaches and maintains steady-state concentration within 72 hours Appropriate pharmacokinetic profile with or without food
Potential Reduced Treatment Burden / Enhanced Patient Convenience	<ul style="list-style-type: none"> 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 get treated on-demand only and graduate to prophylaxis as attack frequency increases (commonly after puberty). To our knowledge, we are the only company that will offer this option to patients.



We plan to develop separate products for on-demand and prophylactic use, PHVS416 and PHVS719 respectively, with both products utilizing the same active ingredient, deucricitbant. PHVS416 will be a softgel capsule, and PHVS719 will be an extended-release tablet. We reported topline data from our RAPiDe-1 Phase 2 clinical trial of PHVS416 acute treatment in December 2022 and topline data from our CHAPTER-1 Phase 2 clinical trial for prophylaxis in December 2023. We also reported data from a Phase 1 clinical trial with PHVS719 in 2022 showing once-daily pharmacokinetics and tolerability of the extended-release formulation.

Expansion of the Portfolio

Our goal is to expand our portfolio with additional programs addressing other BK-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;
- Deucricitbant is an orally available product candidate with a clinically validated mechanism of action that addresses serious unmet medical need in HAE;

8 [Table of Contents](#)

- Deucricitbant has demonstrated physicochemical properties suitable to formulations as both an on-demand product candidate, PHVS416, and a distinct prophylactic product candidate, PHVS719;
- Deucricitbant, 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 BK-blocking pharmacodynamic effect in humans;
- We wholly own intellectual property – including granted and pending patent applications – covering deucricitbant and additional molecules, formulations and use; and
- Our scientific experience allows us to leverage deep insight and experience in the bradykinin-B2-receptor pathway to expand our portfolio into other BK-mediated angioedema and BK-mediated diseases beyond angioedema.

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 PHVS416 and PHVS719 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 deucricitbant through clinical development for on-demand treatment of HAE utilizing a fast-onset formulation, known as PHVS416.* We intend to develop and commercialize PHVS416 as a fast-acting, orally available, potent inhibitor and selective treatment for acute HAE
- *Advance the development of deucricitbant for prophylactic treatment of HAE utilizing an extended-release formulation, known as PHVS719.* We intend to advance PHVS719 through clinical development as an extended-release prophylactic treatment of HAE. We plan to leverage our clinical data and experience from the development of PHVS416 in the on-demand setting to expedite our efforts in the prophylactic setting. We expect the efficacy, safety and PK data from our Phase 2 trials RAPIDE-1 and CHAPTER-1 of PHVS416 to help select and refine our prophylactic dose for the PHVS719 clinical trials.
- *Expand the range of bradykinin-mediated angioedema indications to which PHVS416 and PHVS719 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. 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 PHVS416 and PHVS719 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 BK-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 PHVS416 and PHVS719 in the United States, Europe and certain other countries. As we advance towards regulatory approval for our product candidates, we will 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-esterase inhibitor protein C1-INH. Deficiency or malfunction of C1-INH leads to uncontrolled synthesis and activity of plasma kallikrein and unconstrained BK production. Excessive BK 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, angiotensin-1 or kininogen-1. Moreover, bradykinin-induced acute attacks of angioedema can occur idiopathically in individuals for which a hereditary cause has not yet been identified. Excessive amounts of BK can also be caused by increased circulation of estrogens, reduced C1-INH levels due to underlying diseases, reduced elimination of BK, or through use of medications such as angiotensin-converting enzyme, or ACE, inhibitors and tissue plasminogen activator, or tPA.

9 Table of Contents

Excessive BK 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 present in young children and may take 5-10 years or 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 an overwhelming desire for an oral therapy. We believe that a safe and effective oral agent has the potential to transform treatment for this disease. 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 deucricbant 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. 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 the clinical investigation and new treatment development. Consequently, there are still no treatments approved for hereditary angioedema patients with normal C1-INH or AAE due to C1-INH deficiency, who are unresponsive to conventional antihistamine/glucocorticoid treatment and have a high unmet medical need for effective modern therapies. Recently, clinical research for non-histaminergic angioedema has made significant progress. Similar to Type 1 or 2 HAE, the kinin pathway potentially plays a critical role in the underlying pathophysiology of non-histaminergic angioedema, for example, bradykinin has been shown to be elevated in plasma from non-histaminergic angioedema patients during acute attacks and several clinical reports indicate that icatibant has successfully treated acute attacks in either hereditary angioedema patients with normal C1-INH or AAE due to C1-INH deficiency patients. All these provide strong rationales to expand the development PHVS416 and PHVS719 to these types of BK-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.

Deucricitbant

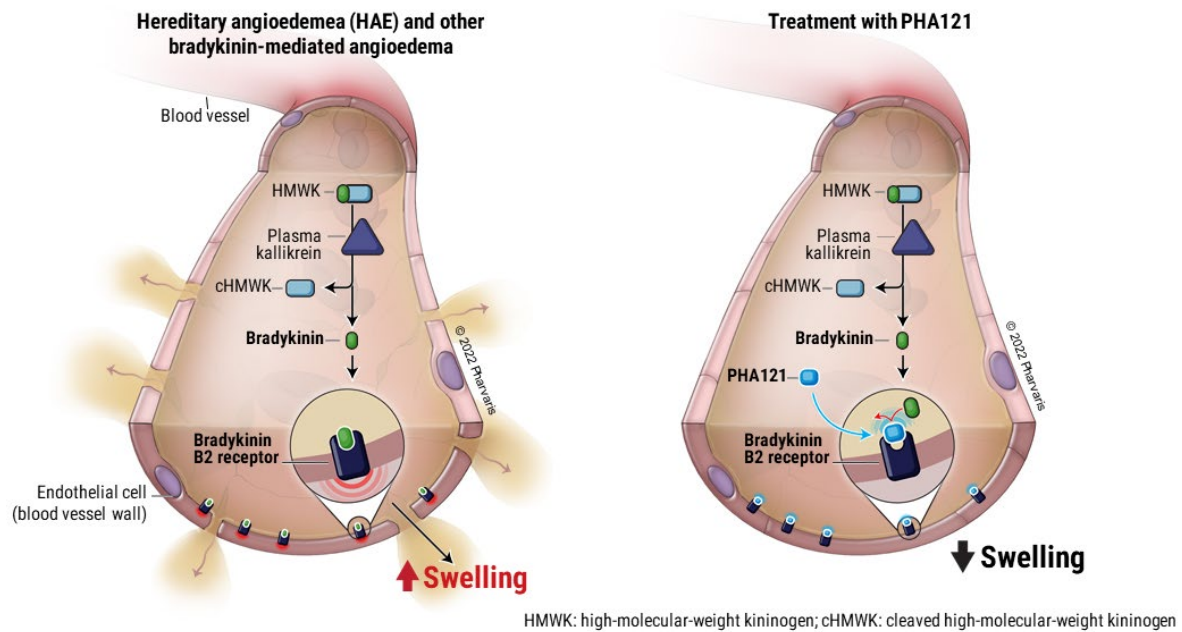
Overview

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 potentially 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, leading to plasma extravasation and subcutaneous or submucosal tissue swelling typical of an angioedema attack.

As the figure below illustrates, treatment with deucricitbant, 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. Deucricitbant therefore has the therapeutic potential for both acute on-demand treatment and long-term prevention of attacks in patients with bradykinin-mediated angioedema.



Deucricitbant combines the preclinical selectivity of bradykinin-B2-receptor antagonism with oral bioavailability and acceptable exposure upon a single dose. Deucricitbant 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 BK-mediated angioedema.

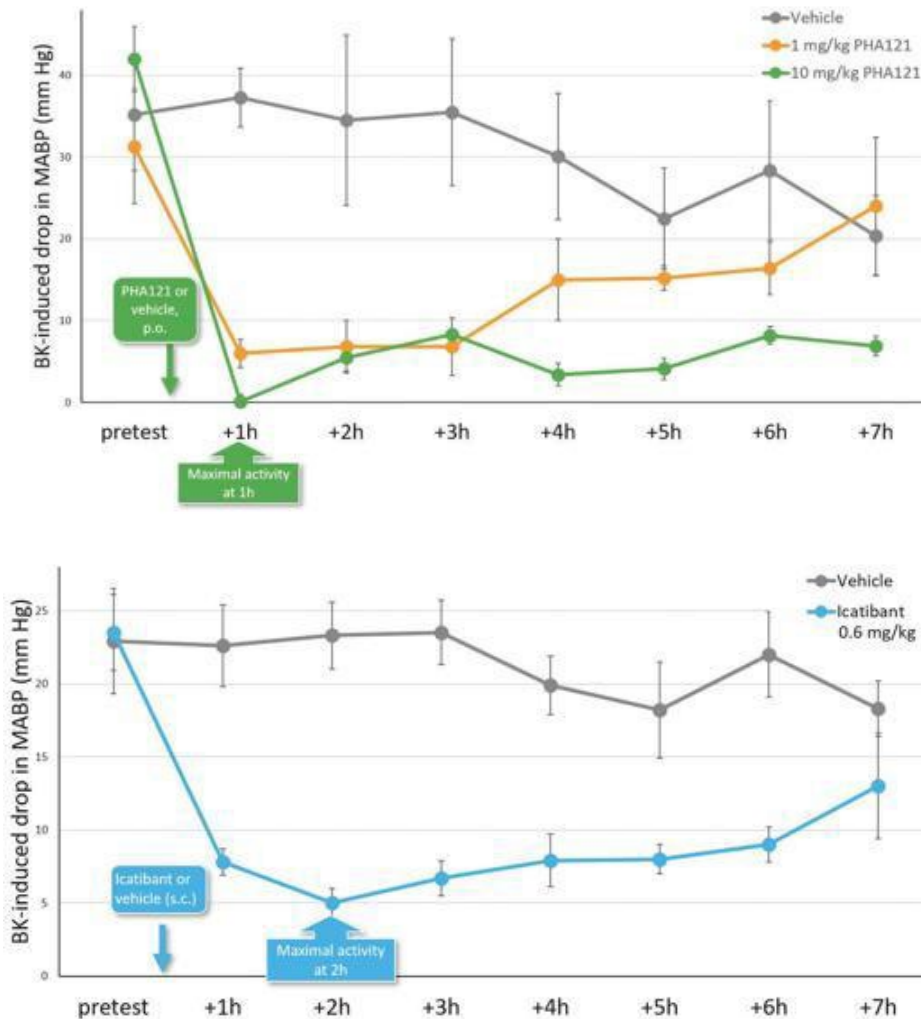
Deucricitbant is an orally bioavailable competitive antagonist of the bradykinin-B2-receptor with high affinity and high antagonist potency. Deucricitbant has been observed to be a potent inhibitor *in vitro* as assessed using human recombinant bradykinin-B2-receptors (150 pM); *ex vivo* as studied against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

Deucricitbant 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), deucricitbant showed clear dose-dependent activity. While

11 [Table of Contents](#)

differences between human and monkey PK prevent direct extrapolation to human dose, deucricitbant 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 deucricitbant in a clinical trial but have compared the published data for icatibant to data from our Phase 1 clinical trial of deucricitbant. 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



In a published study conducted by the Company, a dose of 0.6mg/kg sc icatibant was used in monkeys, as PK data indicated that this dose would provide an exposure (C_{max} 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 (C_{max} 979 ng/mL, AUC 2,191 ng*h/mL). The dose was found to effectively antagonize the BK 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 measure time point, two hours after dosing. The vehicle in the icatibant study was saline.

Deucricitbant inhibited the BK-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 BK-induced changes in MABP at two hours after dosing.

Nonclinical Safety

The conducted nonclinical package for deucricitbant 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. Deucricitbant 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 in each species. Deucricitbant 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,

12 [Table of Contents](#)

male and female fertility studies showed no adverse effects of deucricitbant 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 deucricitbant 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 deucricitbant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucricitbant 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 BK 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-deucricitbant 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 dose 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
C015	Confirmatory XR PK	Open-label, multiple doses to assess PK and safety of extended-release formulation	Ongoing
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 deucricitbant	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	Bioavailability study	Open label, randomized, two-period, cross-over single-dose study under fasting condition	Planned
Phase 2/3			
C201 RAPIDe-1	PHVS416 on-demand	Phase 2, randomized, double blind, placebo-controlled, dose ranging study to assess safety and efficacy	Completed
C303 RAPIDe-2	PHVS416 on-demand open-label extension	Phase 2/3, Extension Study to evaluate the safety of long-term on-demand treatment with deucricitbant for acute HAE attacks	Ongoing
C301 CHAPTER-1	PHVS416 prophylaxis	A two-part Phase 2, randomized, double blind, placebo-controlled dose ranging study to Part 1: assess safety and efficacy of prophylactic treatment with deucricitbant and Part 2: evaluate long-term safety and efficacy for prophylactic treatment with deucricitbant	Ongoing

13 [Table of Contents](#)

C306 RAPIDe-3	PHVS416 on demand	A Phase 3, Randomized, Double-blind, Placebo-controlled, Cross-over Study of Oral Deucricitbant Soft Capsule for On-Demand Treatment of Attacks in Adolescents and Adults with Hereditary Angioedema	Ongoing
C305 CHAPTER-3	PHVS719 prophylaxis	A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Orally Administered Deucricitbant Extended-Release Tablet for Prophylaxis to Prevent Angioedema Attacks in Adolescents and Adults with Hereditary Angioedema	Planned
C307 CHAPTER-4	PHVS719 prophylaxis open-label extension	A Phase 3, Long-term, Open-label Study of Orally Administered Deucricitbant Extended-release Tablet for Prophylaxis to Prevent Angioedema Attacks in Adolescents and Adults with Hereditary Angioedema	Planned

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

Deucricitbant-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 deucricitbant in healthy subjects. A total of 52 subjects received single ascending oral doses of deucricitbant 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 and no orthostatic hypotension linked to deucricitbant groups occurred. The overall incidence of AEs was similar between the placebo and deucricitbant. Treatment-related AEs were reported for three subjects who received deucricitbant (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 deucricitbant in the dose range of 1 mg to 22 mg for C_{max}, AUC_{last} and AUC_{inf}. Median t_{max} 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)	C _{max} (ng/mL)	C _{0.25h} (ng/mL)	C _{12h} (ng/mL)	T _{max} (h)	t _{1/2} (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 deucricitbant: after a 22 mg dose, the mean C_{max} of deucricitbant was lower (~32%) while AUC_{inf} was higher (~42%) when deucricitbant was administered after a high calorie, high-fat breakfast (fed conditions) compared to administration under fasted conditions. While the median t_{max} of deucricitbant was delayed by approximately two hours after administration under fed conditions, the plasma concentration for deucricitbant 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 deucricitbant 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 deucricitbant in a bradykinin challenge model, which was designed to demonstrate deucricitbant-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 deucricitbant 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.

14 [Table of Contents](#)

In the bradykinin challenge, we assessed the inhibition of bradykinin effects at single doses of 12 and 22 mg deucricitabant. Bradykinin was injected intravenously before deucricitabant to calibrate each subject's response, and then at 1, 4, 8, 12 and 24 hours after dosing with deucricitabant. 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 deucricitabant, this cardiovascular response was dampened to an extent depending on the plasma concentration of deucricitabant.

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 BK challenge are provided in the table below. Deucricitabant 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 deucricitabant 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 measurements*.

Composite average	deucricitabant	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 deucricitabant with that of icatibant. However, we have not conducted a head-to-head comparison of icatibant to deucricitabant in a clinical trial but have compared the published data for icatibant to data from our Phase 1 and Phase 2 clinical trial of deucricitabant. 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 deucricitabant leads us to project that due to deucricitabant's longer half-life, we believe deucricitabant will stay above these therapeutic targets for much longer than icatibant. The 12 mg dose of deucricitabant showed rapid absorption and the plasma exposure then stayed above EC50 for 10-12 hours and above the EC85 for 7 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).

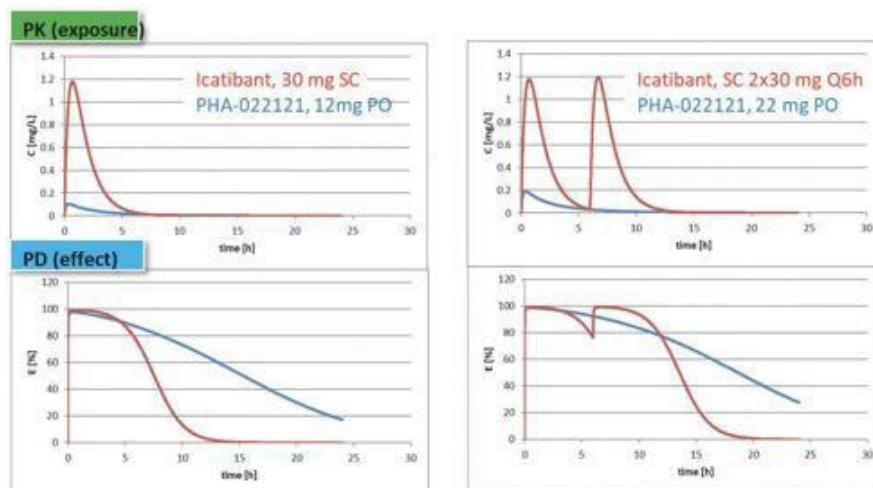
The table below compares 30 mg of icatibant to 12 mg and 22 mg of deucricitabant based on BK-challenge modeling and simulation.

Response	icatibant 30 mg	deucricitabant 12 mg (oral)	deucricitabant 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 deucricitabant 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 deucricitabant 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-

15 Table of Contents

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.



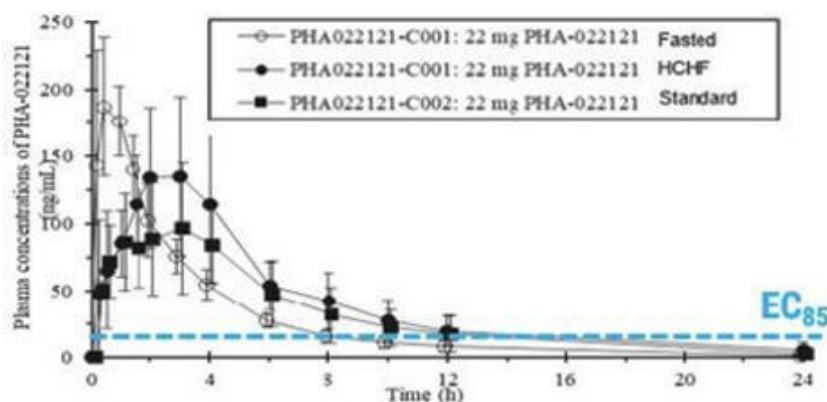
In conclusion, deucricitbant was well tolerated when administered orally at the doses tested without any dose-limiting toxicity. Deucricitbant was rapidly absorbed in either fasting or fed conditions and showed dose proportional PK for deucricitbant. The BK challenge demonstrated that deucricitbant potently 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 deucricitbant after a standard caloric meal and 40 mg in fasting conditions. A total of 32 subjects received either deucricitbant, with respect to 24 subjects, or placebo, with respect to 8 subjects.

The trial results showed that deucricitbant 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 deucricitbant 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, deucricitbant showed dose-proportional PK with a 2.4-fold increase for mean Cmax and AUC0-24h. Administration of deucricitbant 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 deucricitbant 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 deucricitbant Fasted	22 mg of deucricitbant HCHF	22 mg of deucricitbant 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

16 [Table of Contents](#)

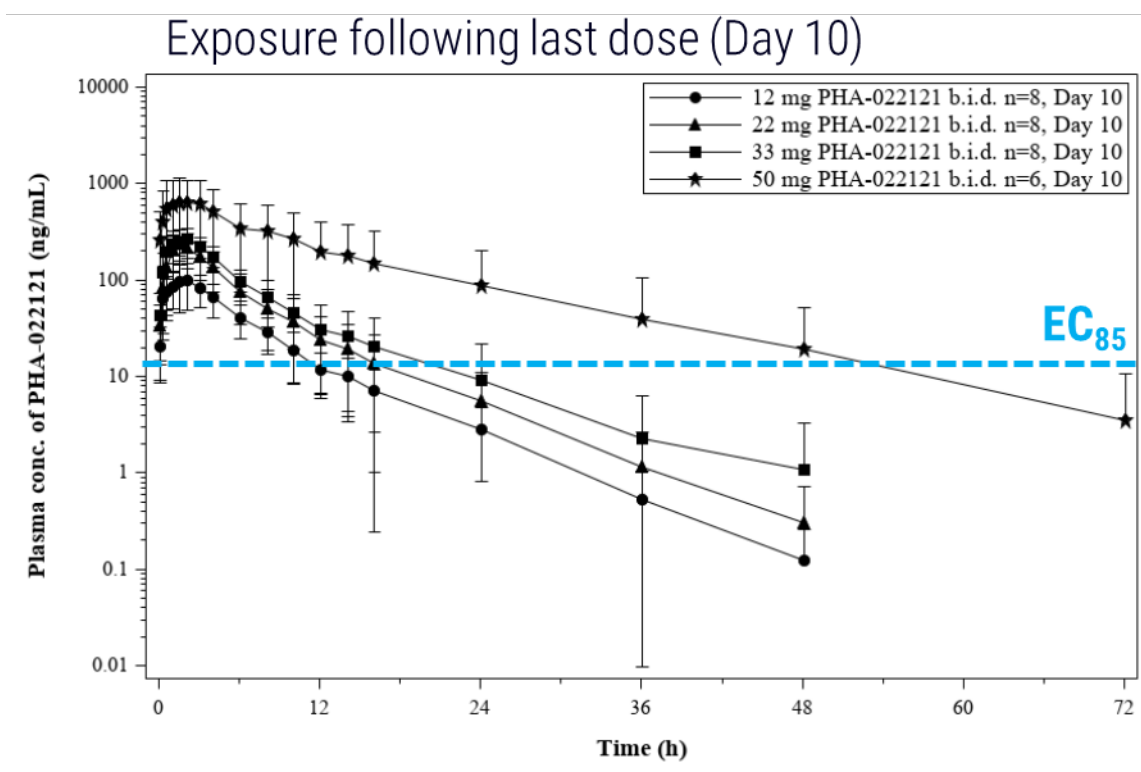
PHA121-C004 (DDI-CYP3A4 inhibitor, itraconazole, interaction)

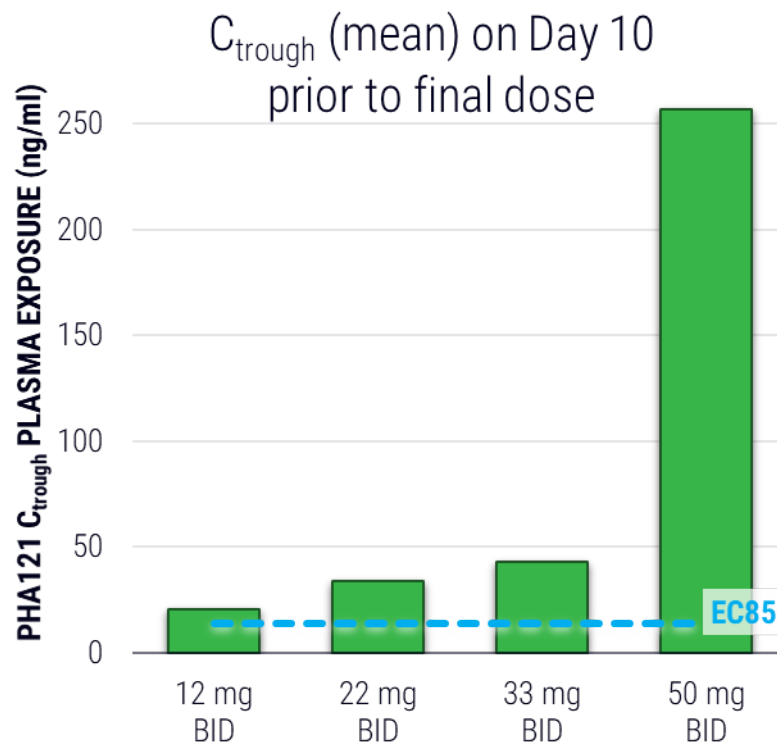
Cytochrome P450 3A4 (CYP3A4) plays an important role in the metabolism of deucricitbant. Deucricitbant-C004 was designed as an open-label, single sequence crossover drug-drug interaction trial to evaluate the effect of multiple doses of itraconazole, a potent CYP3A4 inhibitor, at steady-state on the PK of a single dose of deucricitbant 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 deucricitbant in healthy adult subjects. The secondary objective of this study was to evaluate the safety and tolerability of deucricitbant 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 deucricitbant was well tolerated with no drug-related adverse events reported. Preliminary analyses show that the exposure of deucricitbant increased when co-administered with itraconazole, as expected from *in vitro* data showing that deucricitbant is a substrate of CYP3A4. Other potential drug-drug interactions will be further assessed by the deucricitbant-C005 cocktail interaction study and *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 deucricitbant in healthy subjects, which demonstrated deucricitbant'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 deucricitbant and two subjects received placebo, except for the final cohort with six subjects receiving deucricitbant and two subjects receiving placebo. The trial evaluated multiple ascending doses of twice daily for 10 days to establish safety and tolerability and to assess the PK characteristics of deucricitbant after standard caloric meals. Deucricitbant was supplied as an oral solution.

The study showed deucricitbant 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 deucricitbant were achieved in day 1 and steady-state plasma concentrations were reached within 72 hours.





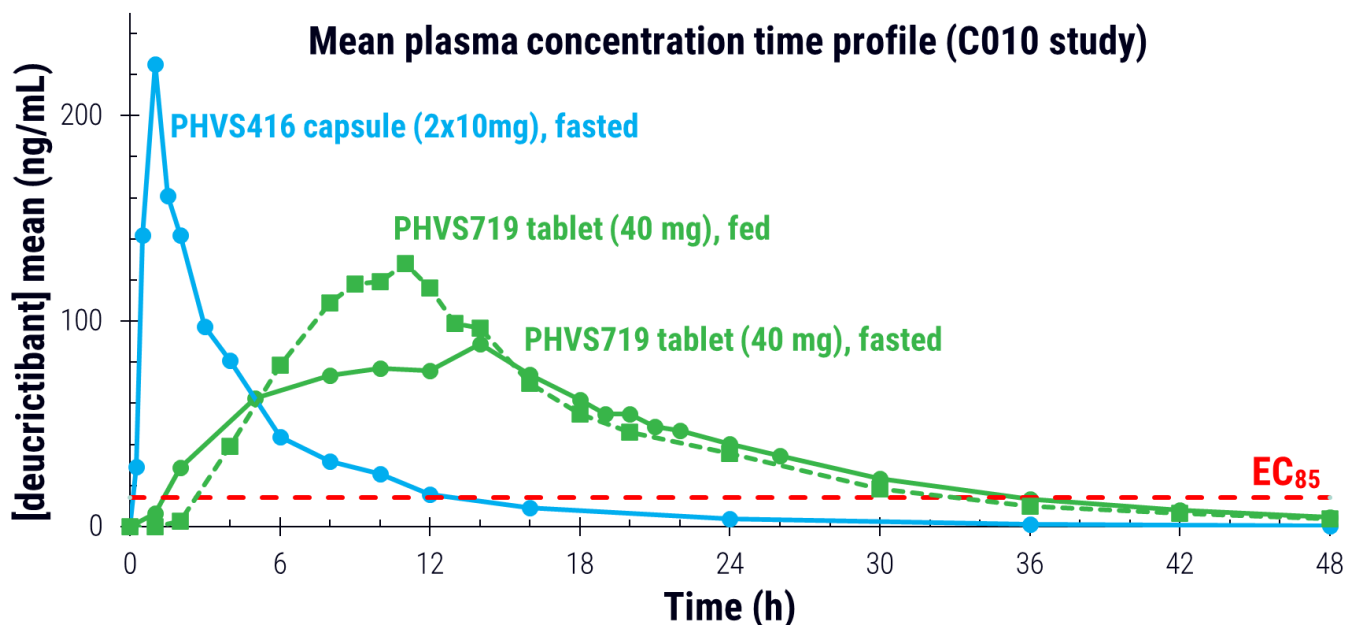
PHA121-C010 (SD)

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 PHVS416 without food. The study included 8 healthy volunteers who received in randomized order a single dose of PHVS416 (20 mg, as two 10-mg softgel capsules) without food, a single tablet of PHVS719 XR1 (20 mg) without food; a single tablet of PHVS719 XR1 (20 mg) with a high-calorie, high-fat meal; a single tablet of PHVS719 XR2 (40 mg) without food; and a single tablet of PHVS719 XR2 (40 mg) with a high-calorie, high-fat meal.

The study showed PHVS416 and PHVS719 were well tolerated. During the study, there were no SAEs or severe treatment-emergent adverse events (TEAEs) reported.

The pharmacokinetic profile observed for PHVS416 confirmed that the softgel capsule formulation under fasting conditions achieved rapid exposure of the deucricitbant active ingredient consistent with previous pharmacokinetic studies using deucricitbant 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 PHVS719 (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 deucricitbant using PHVS719 (40 mg) is similar to that observed in Phase 1 studies with PHVS416 softgel capsules 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 PHVS719 is consistent with a true extended-release formulation designed to provide long-term exposure to deucricitbant. In particular, PHVS719 appears to be suitable for once-daily dosing.



PHA121-C201 (RAPIDe-1 On-Demand)

The availability of an immediate-release softgel capsule formulation, PHVS416, 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 PHVS416 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 PHVS416 softgel capsule for the acute 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 PHVS416 and placebo. The study compared symptom relief during HAE attacks and the safety of each dose of PHVS416 with placebo. In Part I of the study, participants in a non-attack state received the assigned single dose of PHVS416 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 PHVS416 or placebo.

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 PHVS416 significantly reduce attack symptoms. 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 PHVS416 significantly shortens the time to onset of symptom relief by a $\geq 30\%$ reduction in VAS-3 score from the pre-treatment score, decreases time to a $\geq 50\%$ 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 PHVS416 also used substantially less rescue medication compared to placebo.

PHVS416 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 PHVS416 30mg (2.8%) and one treatment-related adverse event was reported for one attack treated with placebo (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 deucricitbant 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 deucricitbant (20 mg/day or 40 mg/day) or placebo for 12 weeks of treatment. Deucricitbant immediate-release capsule (PHVS416) was dosed twice-a-day as a proof-of-concept for the once-daily deucricitbant extended-release tablet (PHVS719), 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.

19 [Table of Contents](#)

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 deucricitabant. In the analysis of the secondary endpoints, deucricitabant 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 deucricitabant treatment also experienced a meaningful improvement in their quality of life.

Throughout 12 weeks of treatment in CHAPTER-1, both dose regimens of deucricitabant (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.

Future Development Path

We intend to develop deucricitabant for on-demand and prophylactic indications in parallel using two different product formulations, with clinical trials in the on-demand setting commencing first in order to provide critical data for further development for the prophylaxis indication.

On-Demand

The availability of an immediate-release softgel capsule formulation, PHVS416, 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 PHVS416 softgel 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 of PHVS416 in acute treatment of HAE attacks.

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 – 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 (an acute treatment model), we relied on a similar acute-to-prophylactic extrapolation utilized for products in the plasma kallikrein mechanism. 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 deucricitabant in the bradykinin challenge, we believe we can utilize a similar concentration-above-EC50/EC85 approach to predict the required exposure of deucricitabant to control attacks prophylactically.

In addition to the RAPIDe-1 on-demand trial, we also conducted a clinical trial of PHVS416 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 PHVS416 softgel 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 deucricitabant. Patients on deucricitabant 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 plan to conduct a registration-directed randomized, placebo-controlled evaluation in HAE prophylaxis to provide the key efficacy and safety evaluation of prophylactic treatment. We anticipate that PHVS719, as described below, will be included in this pivotal trial, with doses selected based on the PK performance of PHVS719 in Phase 1 trials and CHAPTER-1 outcomes. Additional trials may be required by the FDA, EMA or other regulators even if we receive positive data from RAPIDe-1.

In order to provide a differentiated product featuring more consistent exposure of deucricitabant for the prophylactic setting, we are developing an extended-release, or XR, formulation (PHVS719) that will feature continuous slow release maintaining deucricitabant concentrations above the levels we predict to provide protection against attacks. Deucricitabant has demonstrated properties favorable to the development of XR formulations, and we initiated human pharmacokinetics trials with PHVS719 in 2021 to enable use of this product candidate in the pivotal prophylactic trial. With the results of the C010 study, which were described above, we believe we have identified an extended-release formulation that enables once-daily dosing in a prophylactic setting.

In addition, we also plan to run an open-label extension study in the prophylactic setting with both rollover and non-rollover subjects to collect longer duration safety data, which will be further discussed with FDA and EMA.

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 March 1, 2024, we own three U.S. patents, one European patent and 82 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 62 pending patent applications worldwide, including five pending U.S. applications, 57 pending non-U.S. applications, including applications in Europe and Japan, and three pending PCT applications. The U.S. and national/regional patents and 23 of our pending patent applications contain composition-of-matter claims to the deucricitbant small molecule and derivatives thereof; deucricitbant is the active pharmaceutical ingredient (API) in, and therefore extends our patent applications to, our PHVS416 and PHVS719 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. 11 of our pending applications contain claims directed to the use of deucricitbant in on-demand treatment of HAE and in prophylaxis for HAE, and accordingly extend the patent applications to methods of use of the PHVS416 and PHVS719 product candidates. The granted European patent and 22 of our pending patent applications contain claims directed to the formulation of our PHVS416 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. Three pending international (PCT) applications and one pending national application are directly or indirectly directed to the formulation of our PHVS719 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 issue 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 deucricitbant, 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 "AnalytiCon License"), and a research agreement with AnalytiCon to collaborate for the development of an orally available bradykinin-B2-receptor antagonist. Pursuant to the AnalytiCon License, we acquired a worldwide, exclusive license from AnalytiCon 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 deucricitbant, PHVS416 and PHVS719 are subject to the AnalytiCon License. In consideration for the license, we paid AnalytiCon a non-refundable up-front payment of approximately €0.3 million.

Under the AnalytiCon License, we are required to pay AnalytiCon one-time payments in an aggregate amount of up to €11.4 million upon the achievement of certain development, regulatory, and sales milestones. To date, we have paid AnalytiCon an aggregate amount of approximately €1.2 million (approximately €0.3 million up-front plus €0.9 million in milestone payments). Under the AnalytiCon License, up to €10.5 million in aggregate potential milestone payments remain outstanding. In addition, we will be required to pay AnalytiCon low to

21 [Table of Contents](#)

medium single-digit tiered royalties on direct or indirect net sales of licensed products. The royalties that we are required to pay AnalytiCon 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 AnalytiCon will expire upon the expiry of the last patent of the licensed intellectual property. 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 AnalytiCon. If AnalytiCon were to (a) terminate the AnalytiCon License for cause and (b) exercise contractual remedies available to it thereunder, then we could be required to grant to AnalytiCon an exclusive worldwide license to our intellectual property generated under the collaboration with AnalytiCon for use in all applications, including HAE. In addition, we could be prevented from competing with AnalytiCon 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 deucricitbant API. A robust and scalable synthetic route has been established. All raw materials can be purchased from multiple suppliers. We also collaborate with a leading CDMO for the manufacturing of the on-demand treatment product PHVS416. Another well-established CDMO produces the prophylactic treatment product PHVS719. The two CDMOs that manufacture both PHVS416 and PHVS719 are responsible for packaging and worldwide distribution of other commercial drug products.

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 PHVS416 or PHVS719. 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.
- **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, CSL is developing garadacimab, an anti-factor XIIa mAb for prophylactic treatment, which is delivered subcutaneously or intravenously, and Ionis is developing donidalorsen, an antisense oligonucleotide inhibitor of prekallikrein for prophylactic treatment, which is delivered subcutaneously. Earlier stage products in development are STAR-0215 from Astria, a long-lived monoclonal antibody inhibitor of plasma kallikrein dosed subcutaneously, and two gene therapies – NTLA-2002 from Intellia, using CRISPR technology to knock out the gene for kallikrein, and BMN331 from Biomarin using AAV gene therapy technology to deliver C1-INH protein.

22 Table of Contents

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* 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.

Pharmaceutical development

Laboratory tests are conducted to develop a suitable formulation for clinical use and marketing. Product development includes formulation and stability testing, and a robust product manufacturing process. The conduct of pharmaceutical development must comply with regulations and requirements set by the Competent Authorities, including compliance with GLP.

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

23 [Table of Contents](#)

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 FFDC Act, 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

24 [Table of Contents](#)

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 are 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

25 [Table of Contents](#)

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;

26 [Table of Contents](#)

- 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 product. Accordingly, manufacturers must continue to expend 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-

27 [Table of Contents](#)

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

29 Table of Contents

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

30 Table of Contents

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,

31 [Table of Contents](#)

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

32 [Table of Contents](#)

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 the 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.

33 Table of Contents

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

34 [Table of Contents](#)

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;

35 [Table of Contents](#)

- 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 pharmacoeconomic 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.

36 [Table of Contents](#)

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.

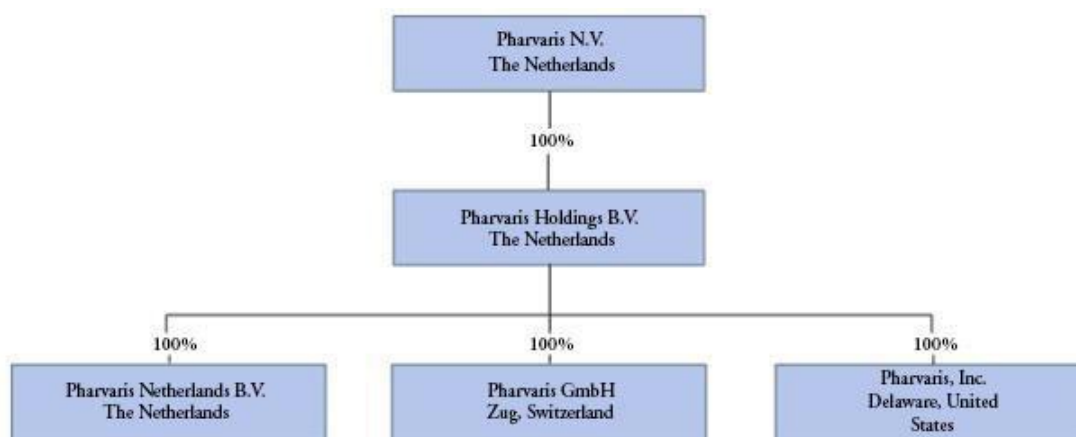
Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented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

2.3 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:



2.4 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 475 square meters is rented through May 31, 2024 and our office space in Zug measuring approximately 58 square meters is rented on a monthly basis.

2.5 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.

37 [Table of Contents](#)

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 clinical-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, deucricitabant (PHA121, PHA-022121), is a novel, small-molecule bradykinin-B2-receptor antagonist for the treatment of hereditary angioedema, or HAE. Bradykinin-B2-receptor inhibition is a clinically validated mechanism for the treatment of HAE, as demonstrated by icatibant, which is a bradykinin-B2-receptor antagonist approved in Europe in 2008 and in the United States in 2011 (as FIRAZYR). PHA121 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 deucricitabant to improve upon the therapeutic profile of existing therapies and, through oral delivery, to provide patients with quality of life and ease-of-administration that is superior to current standard-of-care HAE treatments, which are injectables. We believe deucricitabant has the potential to provide a safe, effective and easy-to-administer option for both acute and prophylactic treatments of HAE, in the form of our PHVS416 (deucricitabant immediate-release (IR)) on-demand rapid exposure product candidate, and for prophylaxis of HAE, in the form of our PHVS719 (deucricitabant extended-release (ER)) small daily dose extended-release product candidate. We believe that our product candidates may address a broader range of angioedema attacks than other available treatments since deucricitabant blocks the actual signal that leads to angioedema (the interaction of bradykinin, or BK with the bradykinin-B2-receptor), rather than an upstream signal. By blocking the action of bradykinin, we can prevent its aberrant signaling regardless of the pathway that generates it.

In our completed Phase 1 trials to date, we have observed that deucricitabant was orally bioavailable and well tolerated at all doses studied, with approximately dose-proportional exposure. We also have successfully demonstrated proof-of-concept through a clinical pharmacodynamics, or PD assessment with the bradykinin challenge, which had been utilized as a validated surrogate assessment for dose selection in the icatibant development program.

We have demonstrated clinical efficacy and tolerability in a Phase 2 study (RAPIDe-1) treating attacks of HAE. The data allowed us to compare the projected therapeutic performance of deucricitabant with that of icatibant. However, we have not conducted a head-to-head comparison of icatibant to deucricitabant in a clinical study. We plan to efficiently progress deucricitabant through clinical development for on-demand and prophylactic use with our on-demand immediate-release product candidate, PHVS416, and prophylactic extended-release product candidate, PHVS719, respectively. We commenced our RAPIDe-1 Phase 2 clinical trial of PHVS416 in February 2021 and reported topline Phase 2 data for the acute treatment of patients with HAE attacks in December 2022. We have also demonstrated clinical efficacy and tolerability in a Phase 2 study (CHAPTER-1) for prophylaxis of HAE attacks. We commenced the CHAPTER-1 Phase 2 clinical trial for prophylaxis in 2021 using twice-daily dosing of the PHVS416 soft capsules and announced positive topline data in December 2023. Our primary objective with this trial was to assess the efficacy and safety profile of PHVS416 dose regimens for prophylactic treatments in HAE patients. In February 2022, we reported Phase 1 clinical data with PHVS719 demonstrating pharmacokinetics of the extended-release formulation and the potential for once-daily dosing. In healthy volunteers, a single dose of PHVS719 was well tolerated with an extended-release profile supporting once-daily dosing.

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. While the impact of COVID-19 on the Company's operations and financial performance has so far been limited, the extent to which COVID-19 may impact our financial condition or results of operations in the future is uncertain. For instance, the ongoing spread of variants of the COVID-19 virus may continue to interrupt, or delay, our clinical trial activities, regulatory reviews, manufacturing activities and supply chain.

The extent to which the COVID-19 pandemic impacts our business will depend on future developments, which are uncertain and cannot be predicted, including new information which may emerge concerning the severity of the COVID-19 pandemic and the actions to contain COVID-19 or treat its impact, including among other things, the effectiveness and outreach of COVID-19 vaccines.

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.

Furthermore, in August 2022, the FDA placed a hold on the clinical trials of deucricitabant 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 deucricitabant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucricitabant for the prophylactic treatment of HAE attacks following review of the full data set from the completed 26-week rodent toxicology study.

38 Table of Contents

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 5, 2023.

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 deucricitibant. Since our inception, we have devoted substantially all of our resources to research and development efforts relating to the development of deucricitibant and our product candidates PHVS416 and PHVS719. 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 PHVS416 and PHVS719, 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 2024 as we continue to focus on the development of our product candidates PHVS416 and PHVS719, as well as explore potential expansion programs. We anticipate that research and development expenses will continue to increase as we continue to progress PHVS416 and PHVS719 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.

39 [Table of Contents](#)

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 and expenses or general and administrative expenses.

The share-based payment expense recorded for the years ended December 31, 2023, 2022 and 2021 were €10.7 million, €11.3 million and €8.2 million respectively.

Comparison of the years ended December 31, 2022 and 2021

A discussion of the financial results for the year ended December 31, 2022 as compared to the year ended December 31, 2021 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, 2022 and 2021" in our annual report on form 20-F, filed with the SEC on April 5, 2023.

Comparison of the years ended December 31, 2023 and 2022

The following table summarizes our loss for the periods indicated:

	For the year ended December 31,		Change	%
	2023	2022 (in €)		
Research and development expenses	(65,575,030)	(57,375,574)	(8,199,456)	14%
General and administrative expenses	(31,338,590)	(29,339,034)	(1,999,556)	7%
Total operating expenses	(96,913,620)	(86,714,608)	(10,199,012)	12%
Finance (expense) income	(2,912,643)	11,061,138	(13,973,781)	(126)%
Loss before income tax	(99,826,263)	(75,653,470)	(24,172,793)	32%
Income taxes	(1,048,805)	(679,087)	(369,718)	54%
Loss for the period	(100,875,068)	(76,332,557)	(24,542,511)	32%

Research and development expenses

	For the year ended December 31,		Change	%
	2023	2022		
	(in €)			
Personnel expenses	(19,132,307)	(13,334,350)	(5,797,957)	43%
Clinical expenses	(30,690,293)	(27,653,658)	(3,036,635)	11%
Nonclinical expenses	(8,977,187)	(4,853,822)	(4,123,365)	85%
Manufacturing costs	(6,500,986)	(11,181,355)	4,680,369	(42)%
Intellectual property costs	(274,257)	(352,389)	78,132	(22)%
Total research and development expenses	(65,575,030)	(57,375,574)	(8,199,456)	14%

Research and development expenses increased by €8.2 million in 2023, or 14% from €57.4 million for the year ended December 31, 2022 to €65.6 million for the year ended December 31, 2023.

For the years ended December 31, 2023 and 2022, personnel expenses were €19.1 million and €13.3 million, respectively. This represents an increase of €5.8 million, or 43%. The increase is mainly driven by the growth of the organization and yearly merit adjustments. Personnel expenses in 2023 included an amount of €4.6 million (2022: €4.2 million) of share-based compensation.

For the years ended December 31, 2023 and 2022, clinical expenses were €30.7 million and €27.7 million, respectively. This represents an increase of €3.0 million, or 11%. The increase in clinical expenses is primarily due to the expansion from the Phase 1 clinical program to our Phase 2 clinical program. The Phase 2 program involves two global, placebo-controlled clinical studies with dosing over multiple months. In addition, Open Label Extension studies have been initiated and have been running for the two programs.

For the years ended December 31, 2023 and 2022, nonclinical expenses were €9.0 million and €4.9 million, respectively. This represents an increase of €4.1 million, or 85%. The increase in nonclinical expenses is primarily due to the additional studies related to the 26-week rodent toxicology study intended to address the clinical hold in the U.S.

For the years ended December 31, 2023 and 2022, manufacturing costs were €6.5 million and €11.2 million, respectively. This represents a decrease of €4.7 million, or 42%. Manufacturing costs were lower mainly due to decreased expenses for drug substance manufacturing, which took place in 2022 as preparation for our clinical trials in 2023 and that resulted in lower manufacturing activities in 2023. Some activities, like pre-validation, were also postponed to 2024 due to emerging development activities.

General and Administrative Expenses

	For the year ended December 31,		Change	%
	2023	2022		
	(in €)			
Personnel expenses	(13,314,359)	(13,484,996)	170,637	(1)%
Consulting fees	(602,110)	(898,435)	296,325	(33)%
Professional fees	(4,689,462)	(3,972,771)	(716,691)	18%
Accounting, tax and auditing fees	(2,029,554)	(1,652,995)	(376,559)	23%
Insurance, facilities and office expenses	(6,031,513)	(6,443,709)	412,196	(6)%
Travel expenses	(1,797,588)	(1,105,961)	(691,627)	63%
Other expenses	(2,874,004)	(1,780,167)	(1,093,837)	61%
General and administrative expenses	(31,338,590)	(29,339,034)	(1,999,556)	7%

General and administrative expenses increased by €2.0 million, or 7% from €29.3 million for the year ended December 31, 2022 to €31.3 million for the year ended December 31, 2023. The increase in general and administrative expenses was mainly driven by the growth of our organization and increasing costs related to our commercial buildout.

For the years ended December 31, 2023 and 2022, personnel expenses were €13.3 million and €13.5 million, respectively. This represents a decrease of €0.2 million, or 1%. Personnel expenses in 2023 included an amount of €6.1 million (2022: €7.1 million) of share-based compensation. The increase of personnel expenses, net of share-based compensation is mainly driven by the growth of the organization and yearly merit adjustments.

Finance (expense) / income - net

Finance (expenses) income - net, for the year ended December 31, 2023 and 2022 were €(2.9) million and €11.1 million respectively, a change of €14.0 million. The amount mainly relates to unrealized foreign exchange gains and losses, which is mostly the result of translating the Company's bank balances held in USD to EUR. The foreign exchange rates did not develop in favor of the Company in 2023.

41 [Table of Contents](#)

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, 2023 of approximately €325.0 million (2022: €182.3 million; 2021: €95.7 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:

	November 15, 2023	April 6, 2023	June 1, 2022	April 1, 2022	January 1, 2022	July 1, 2021	June 25, 2021 Option 1	June 25, 2021 Option 2	February 4, 2021	January 1, 2021
Number of options	90,000	846,000	120,000	552,500	70,000	150,000	14,000	88,000	873,000	107,000
Fair value of the options	€ 12.27	€ 5.92	€ 11.89	€ 11.50	€ 9.08	€ 10.50	€ 10.90	€ 13.73	€ 11.88	€ 5.06
Fair value of the ordinary shares	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65	€ 14.67	€ 15.46	€ 15.46	€ 16.69	€ 7.25
Exercise price	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65	€ 14.67	€ 16.74	€ 2.38	€ 16.69	€ 7.25
Expected volatility (%)	100%	100%	80%	80%	85%	85%	85%	85%	85%	85%
Expected life (years)	6.1	6.1	6.1	6.1	6.1	6.1	6.1	4.6	6.1	6.0
Risk-free interest rate (%)	4.6%	3.6%	3.0%	2.6%	1.4%	1.2%	1.2%	-0.5%	0.8%	-0.6%

Expected volatility in 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 German government Strip bonds or 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 €100.9 million during the year ended December 31, 2023 and €76.3 million during the year ended December 31, 2022. 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, 2023, 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 with SVB Securities LLC, or SVB Securities, pursuant to which we may sell ordinary shares having an aggregate offering price of up to \$75 million from time to time through SVB Securities.

As of December 31, 2023, 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. Our understanding is that SVB Securities was not impacted by the Silicon Valley Bank ("SVB") receivership proceedings.

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).

As of December 31, 2023 we held cash and cash equivalents of €391.2 million. Of the cash on hand, €65,567 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;

43 [Table of Contents](#)

- 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 financings, 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 to 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 SVB. As of April 10, 2024, 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, 2023 and December 31, 2022

A discussion of our cash flows for the year ended December 31, 2022 as compared to the year ended December 31, 2021 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, 2022 and 2021” in our annual report on form 20-F, filed with the SEC on April 5, 2023.

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,		Change	%
	2023	2022		
Net cash flows used in operating activities	(93,049,093)	(67,162,634)	(25,886,459)	39%
Net cash flows used in investing activities	(89,984)	(124,296)	34,312	(28)%
Net cash flows provided by financing activities	325,393,000	8,650,368	316,742,632	3662%
Net increase (decrease) in cash and cash equivalents	232,253,923	(58,636,562)	290,890,485	(496)%
Cash and cash equivalents at beginning of period	161,837,429	209,353,132	(47,515,703)	(23)%
Effect of exchange rate changes	(2,859,715)	11,120,859	(13,980,574)	(126)%
Cash and cash equivalents at end of period	391,231,637	161,837,429	229,394,208	142%

Operating activities

Net cash flows used in operating activities, reflects 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.

44 [Table of Contents](#)

Net cash flows used in operating activities increased by €25.9 million or 39%, from €67.2 million for the year ended December 31, 2022 to €93.0 million for the year ended December 31, 2023. The change is primarily due to the increase in research and development expenses and other operating expenses and to progression made in the development programs and the growth of our organization.

Investing activities

Net cash flows used in investing activities are substantially unchanged for the year ended December 31, 2023 compared to the year ended December 31, 2022.

Financing activities

Net cash flows provided by financing activities increased by €316.7 million from €8.7 million for the year ended December 31, 2022 to €325.4 million for the year ended December 31, 2023. 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. Net cash provided by financing activities in the year ended December 31, 2022 consisted primarily of the receipt of €9.6 million received from the sale of ordinary shares, offset by transaction costs of €0.8 million and the payment of principal portion of lease liabilities of €0.1 million.

Disclosure of contractual obligations

The Group (as defined below) has entered into research and development commitments in relation to the development of the Group's oral bradykinin-B2-receptor antagonist amounting to a total of €49 million as of December 31, 2023 (2022: €28 million), of which €44.8 million is committed in the year ending December 31, 2024. The amount for research and developments 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 agreement we have entered into with AnalytiCon to license intellectual property.

Under the AnalytiCon License, up to €10.5 million in aggregate potential milestone payments remain outstanding. In addition, we will be required to pay AnalytiCon low to medium single-digit tiered royalties on direct or indirect net sales of licensed products. The royalties that we are required to pay AnalytiCon 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 chapter 2.2.

D. Trend information

For a discussion of trend information, see chapter "ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS." in our annual report on form 20-F, filed with the SEC on April 8, 2024.

2.6 Material subsequent events

See Note 23 (*Events after the reporting period*) to the consolidated financial statements included in chapter 9 of this report (the "**Consolidated Financial Statements**") for an overview of events which do not need to be discussed in the Company's statutory annual accounts and which might influence the Company's outlook.

There are no other events which might influence the Company's outlook and which are not discussed in the statutory annual accounts included in this report.

3. Risk factors

3.1 Summary Risk Factors

The principal risks and uncertainties which the Company faces include the risks and uncertainties summarized in this chapter 3.1. See chapter 3.2 of this report for additional detail and additional risks and uncertainties which the Company faces.

- 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 such as the COVID-19 pandemic and political instability such as the current 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 PHVS416 and PHVS719, 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 deucricitibant immediate-release (PHVS416) and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucricitibant 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 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 deucricitibant 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.
- We have identified material weaknesses in our internal control over financial reporting. If we are unable to successfully remediate these material weaknesses and to maintain an effective system of 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.

46 [Table of Contents](#)

- 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 to AnalytiCon Discovery GmbH, or AnalytiCon, under the terms of the agreement pursuant to which we acquired certain of our core intellectual property, AnalytiCon 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.

3.2 Risk factors

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.

47 Table of Contents

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

48 [Table of Contents](#)

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.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to successfully remediate these material weaknesses and to maintain an effective system of 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. Any failure to implement the required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. 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. 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 consolidated financial statements as of and for the fiscal year ended December 31, 2023, 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 us maintaining sufficient personnel commensurate with our accounting and reporting requirements, and our ability 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 and (iii) design and maintain controls over the preparation and review of journal entries and financial statements, including maintaining appropriate segregation of duties.

Although several oversight and control activities are performed, not all activities are formalized and documented properly throughout the year. In addition, where control activities are dependent on information used in a control, we have not always performed or documented controls to determine the completeness and accuracy of such information. We also did not always have controls in place to monitor control activities and identify control deficiencies. During fiscal year 2023, we developed and implemented a remediation plan to address the material weaknesses identified in previous years. The remediation actions implemented during fiscal year 2023 mainly addressed the general setup for an Internal Control Over Financial Reporting system in (i) improving the composition and expertise of accounting and financial reporting personnel; (ii) further developing and documenting our scoping of key processes and risk and control matrices; (iii) finalizing our drafted formal policies on our internal controls system; (iv) implementing a new accounting system throughout fiscal year 2023 that became operational starting January 2024 which is improving the IT general controls environment, increasing the number of application controls and reducing the manual nature of execution of key controls throughout significant business processes; (v) developing a risk management policy to set out the processes, methods, and tools used to manage the risks within the Company and a risk inventory to grade the consequences and likelihood of occurrence of each risk and (vi) developing awareness and training plans for risk and control owners.

As we continue with the remediation of our material weaknesses, we may determine that additional or other measures may be necessary to address and remediate the material weaknesses, depending on the circumstances and the Company needs. We will not be able to fully remediate these material weaknesses until these steps have been completed and have been operating effectively for a sufficient period of time. We cannot assure you that we will be able to successfully remediate these material weaknesses or that other 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). However, our independent registered public accounting firm was not required to attest to the effectiveness of our internal

49 [Table of Contents](#)

control over financial reporting and will not be so required for as long as we are an “emerging growth company” under the JOBS Act. We could be an “emerging growth company” until December 31, 2026 (the last day of our fiscal year following the fifth anniversary of our initial public offering in February 2021) although depending on certain conditions related to our market capitalization and free float, we may lose “emerging growth company” status in 2024. 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 depends 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 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 recently lifted clinical holds. Moreover, we have established proof-of-concept for deucricitab 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 deucricitabant 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 deucricitabant 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 deucricitabant for the on-demand treatment of HAE in June 2023. In January 2024, the FDA lifted the clinical hold on the IND application for deucricitabant 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 PHVS416 and PHVS719 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 such as the COVID-19 pandemic, (ii) the escalation of the ongoing conflict between Russia and Ukraine and (iii) the Hamas attack against Israel and the ensuing war;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up, including due to (i) pandemics such as the COVID-19 pandemic, (ii) the escalation of the ongoing conflict between Russia and Ukraine and (iii) the Hamas attack against Israel and the ensuing war;
- 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.

51 [Table of Contents](#)

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 deucricitibant, including our product candidates PHVS416 and PHVS719, 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 PHVS416 and PHVS719, 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 deucricitibant immediate-release (PHVS416) and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucricitibant 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, PHVS416 and PHVS719, 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 deucricitibant 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 deucricitibant in a clinical trial. We have compared the published data for icatibant to data from our Phase 1 clinical trial of deucricitibant and Phase 2 trial of PHVS416 (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 PHVS416 and PHVS719 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 deucricitibant-containing product candidate, including PHVS416 and PHVS719, 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 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 PHVS416 and PHVS719 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, such as the COVID-19

pandemic, and political 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, such as the COVID-19 virus, 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. For example, in 2020, we experienced an approximate two-month delay in starting the enrollment of our now completed Phase 1 multiple ascending dose study of deucricitibant in healthy volunteers as a result of COVID-19. 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 FDA, EMA and other government agencies caused by 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, 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. For instance, in response to COVID-19, on March 10, 2020, the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Foreign pre-approval and for-cause inspection assignments that are not deemed mission-critical remain temporarily postponed, while those deemed “mission-critical” are being considered for inspection on a case-by-case basis. In addition, regulatory agencies have generally reduced face-to-face interactions relative to the pre-pandemic situation which may impact our ability to reach consensus with regulators. If a prolonged government shutdown occurs, or if global health concerns continue to 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 deucricitibant prophylactic indication (PHVS719). 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, such as the COVID-19 pandemic;
- 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

54 [Table of Contents](#)

effectiveness results in larger-scale pivotal clinical trials. In this Annual Report we discuss the potency of deucricitbant 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 deucricitbant immediate-release (PHVS416) and topline data from our CHAPTER-1 study demonstrating efficacy in our Phase 2 clinical trial of deucricitbant 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. In addition, there is a constrained supply of some types of animals for research and nonclinical studies which has arisen as a consequence of the COVID-19 pandemic. This reduction in supply and the prioritization for COVID-19-related studies have severely restricted the availability of some types of animals for other pharmaceutical development programs and has the potential to significantly delay the nonclinical toxicology and developmental and reproductive toxicity studies.

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 PHVS416 and PHVS719. 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;

55 [Table of Contents](#)

- 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 (deucricitbant), the active ingredient in our PHVS416 and PHVS719 product candidates for treatment of bradykinin-mediated angioedema. Even though we have obtained orphan drug exclusivity for deucricitbant 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 deucricitbant 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, 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. While the Biden administration has proposed to repeal, or delayed implementation of, certain of the actions taken by the Trump administration, 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.

57 [Table of Contents](#)

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 PHVS416 and PHVS719. 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 the 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; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

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

59 [Table of Contents](#)

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 PHVS416 and PHVS719 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 PHVS416 and PHVS719 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 PHVS416 and PHVS719, 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 deucricitab 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 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;

61 [Table of Contents](#)

- 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 PHVS416 and PHVS719, 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 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;

63 [Table of Contents](#)

- 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 to AnalytiCon pursuant to the agreements 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), AnalytiCon 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 AnalytiCon and contractually assigned to us by AnalytiCon, with whom we continue to collaborate for the development of our product candidates. We owe AnalytiCon 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 to AnalytiCon or are otherwise in material breach of certain agreements that we entered into with AnalytiCon (and fail to cure such breaches within a specified time period), and AnalytiCon exercises contractual remedies available to it under such agreements, then we may be required to grant AnalytiCon 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 AnalytiCon 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 AnalytiCon 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 AnalytiCon, 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.

66 [Table of Contents](#)

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 deucricitbant 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

70 [Table of Contents](#)

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

71 [Table of Contents](#)

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

72 [Table of Contents](#)

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 wastes. 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

74 [Table of Contents](#)

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, 2024, our significant shareholders beneficially owned ordinary shares representing approximately 59.01% 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 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

75 [Table of Contents](#)

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 way with which you do not agree and in ways that may not yield a return on your investment.

As of December 31, 2023, we had €391.2 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 53,816,707 ordinary shares outstanding as of April 1, 2024. 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, independent 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.

We are eligible to be treated as an "emerging growth company," as defined in the JOBS Act, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our ordinary shares less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including an exemption from the independent auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act; and to the extent that we no longer qualify as a foreign private issuer, (a) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and (b) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation, including golden parachute compensation. We cannot predict whether investors will find our ordinary shares less attractive if we rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be reduced or more volatile.

We may take advantage of these provisions until such time that we are no longer an emerging growth company. We would cease to be an emerging growth company on December 31, 2026 (the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering in February 2021) or earlier if we have more than \$1.235 billion in annual revenues, are deemed to be a "large accelerated filer" under the rules of the SEC, or issue more than \$1.0 billion of nonconvertible debt over a three-year period. We may also choose to take advantage of some but not all of these reduced burdens. For example, Section 107 of the JOBS Act provides that an emerging growth company can use the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Given that we currently report and expect to continue to report under IFRS, as issued by the IASB. Given that we currently report and expect to continue to report under IFRS as issued by the IASB, we will not be able to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required by the IASB. We have taken advantage of reduced reporting requirements in this Annual Report. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold equity securities.

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 parties 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 being 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 one 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 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 for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

78 [Table of Contents](#)

- 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.

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

79 [Table of Contents](#)

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 2023 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 2024 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 2024 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

80 [Table of Contents](#)

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, such as the COVID-19 pandemic;
- 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 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.

81 [Table of Contents](#)

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 covers 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. Particularly after we are no longer an "emerging growth company" or cease to qualify as a foreign private issuer, we expect to incur significant legal, accounting and other expenses.

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.

4. Controls and Procedures

4.1 Risk management and control systems

As of December 31, 2023, our management, including our Chief Executive Officer and Principal Accounting 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.

82 Table of Contents

Based on such evaluation, our Chief Executive Officer and Principal Accounting Officer concluded that our disclosure controls and procedures were not effective due to material weaknesses in the design of our internal control over financial reporting.

Internal Control over Financial Reporting

We are relying on certain exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We have taken advantage of these reduced reporting requirements in this Annual Report.

Remediation Plan

The remediation actions implemented during fiscal year 2023 mainly address the general setup for an Internal Control Over Financial Reporting system:

- improving the composition and expertise of accounting and financial reporting personnel;
- further developing and documenting our scoping of key processes and risk and control matrices;
- finalizing our drafted formal policies on our internal controls system;
- implementing a new accounting system throughout fiscal year 2023 being operational since January 2024 which is improving the IT general controls environment, increasing the number of application controls and reducing the manual nature of execution of key controls throughout significant business processes;
- developing a risk management policy to set out the processes, methods, and tools used to manage the risks within the Company and a risk inventory to grade the consequences and likelihood of occurrence of each risk; and
- developing awareness and training plans for risk and control owners.

As we continue with the remediation of our material weaknesses, we may determine that additional or other measures may be necessary to address and remediate the material weaknesses, depending on the circumstances and the Company needs. We will not be able to fully remediate these material weaknesses until these steps have been completed and have been operating effectively for a sufficient period of time. We cannot assure you that we will be able to successfully remediate these material weaknesses or that other material weaknesses will not be discovered in the future.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Principal Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based upon criteria established in *Internal Control – Integrated Framework (2013)* by the Committee of Sponsoring Organizations of the Treadway Commission. A material weakness is a deficiency, or combination of control deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected in a timely basis. Based on that evaluation, due to the material weaknesses described below, our management concluded that our internal control over financial reporting was not effective as of December 31, 2023.

In connection with the preparation of our consolidated financial statements as of and for the year ended December 31, 2023, 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.

The material weakness related to formal accounting policies, procedures and controls as well as accounting for complex accounting matters resulted in audit adjustments for the years ended December 31, 2022 and 2021. Additionally, these material weaknesses could result in a material misstatement of substantially all of Pharvaris N.V. consolidated accounts or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected.

83 [Table of Contents](#)

Pharvaris N.V. 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, Pharvaris N.V. 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. The IT deficiencies did not result in any misstatements to the consolidated financial statements, however, the deficiencies, when aggregated, could impact maintaining effective segregation of duties, as well as the effectiveness of IT-dependent controls (such as automated controls that address the risk of material misstatement to one or more assertions, along with the IT controls and underlying data that support the effectiveness of system-generated data and reports) that could result in misstatements potentially impacting all financial statement accounts and disclosures that would not be prevented or detected. Accordingly, Pharvaris N.V. management has determined these deficiencies in the aggregate constitute a material weakness.

Changes in Internal Control over Financial Reporting

Other than the changes to address our material weaknesses described above there have been no changes in internal control over financial reporting that occurred during the period covered by this annual report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

4.2 In control statement

On the basis of reports and information provided to the Board and its committees, the Board is of the opinion that due to the material weaknesses described above, our internal control over financial reporting was ineffective as of December 31, 2023.

On the basis of reports and information provided to the Board and its committees, the Board is of the opinion that:

- this report provides sufficient insight into any failings in the effectiveness of the Company's risk management and control systems;
- the Company's risk management and control systems provide reasonable assurance that the Company's financial reporting does not contain material inaccuracies (other than the material weaknesses described above);
- based on the Company's state of affairs as at the date of this report, it is justified that the Company's financial reporting is prepared on a going concern basis; and
- this report states those material risks and uncertainties that are relevant to the expectation of the Company's continuity for a period of twelve months after the date of this report.

The Board determined that due to the limited size and complexity of the Company no internal audit department had to be established in 2023.

Furthermore, the Board confirms that:

- a) to the best of its knowledge, the statutory annual accounts included in this report give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company and its consolidated subsidiaries taken as a whole; and
- b) this report includes a fair review concerning the position, on the balance sheet date, and the development and performance of the business of the Company and its consolidated subsidiaries taken as a whole, together with a description of the principal risks and uncertainties that they face.

5. Corporate Governance

5.1 Dutch Corporate Governance Code

For the fiscal year to which this report relates, the Dutch Corporate Governance Code 2022 (the "**DCGC**") applied to the Company. The text of the DCGC can be accessed at <http://www.mccg.nl>.

Except as set out below, during the fiscal year to which this report relates, the Company complied with the principles and best practice provisions of the DCGC, to the extent that these are directed at the Board.

- Under the Company's 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 of the Company (the "General Meeting") overrules the binding nature of the nomination (in which case a new nomination will be prepared for a subsequent General Meeting). The Company's articles of association provide that the General Meeting can only pass such resolution by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital. However, the DCGC recommends that the General Meeting should be capable of passing such a resolution by a simple majority of votes cast, representing no more than one-third of the issued share capital.

84 [Table of Contents](#)

- Under the Company's articles of association, directors can only be dismissed by the General Meeting by simple majority of votes cast, 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, we deviate from this recommendation and grant equity awards to our non-executive directors, consistent with U.S. market practice.
- The Pharvaris N.V. 2021 Equity Incentive 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.
- The DCGC recommends that the Board appoints a separate department for the internal audit function. However, the Company did not have any such department in place in 2023. Instead, adequate alternative measures have been taken and the Company has improved on robust internal controls to safeguard our operations and financial reporting. These measures include:
 - Segregation of Duties: We have clearly defined roles and responsibilities to prevent any single individual from having excessive control over critical processes.
 - Regular Performance Reviews: All employees undergo periodic performance evaluations to ensure adherence to policies and procedures.
 - Review and Approval Processes: We have established rigorous approval workflows for financial transactions, ensuring proper oversight.
 - Education and Training: Our staff receives ongoing training on compliance, risk management, and ethical conduct.
 - Engaging External Consultants: Recognizing the importance of independent oversight, we have engaged and external consulting firm to help the Company achieve SOX 404 compliance. This firm assesses our internal controls over financial reporting framework. Their expertise provides an objective evaluation of our processes, obviating the need for an internal audit department.
 - Testing and Verification: External consultants test transactions and review documentation to conclude on the design and execution of the controls.
 - Recommendations: Based on findings of the aforementioned testing and verification, the external consultants provide recommendations for process improvements and risk mitigation.
 - Reporting to the Audit Committee: the Audit Committee is regularly provided with reports on internal controls, enhancing transparency and accountability.
- The DCGC recommends that the Company should have a Stakeholder Dialogue Policy in place. The Company does not have a formal Stakeholder Dialogue Policy in place in because the Company has identified relevant stakeholders and the various channels for dialogue that have already been implemented by the Company. Based on the stakeholder initiatives already in place, the Company agreed that this Policy was not necessary at this time.
- The DCGC recommends that the Company should have a Diversity and Inclusion Policy in place. The Company does not have a formal Diversity and Inclusion Policy in place in which concrete targets in respect of gender diversity are included because of the following reasons:
 - Collecting broader D&I data creates substantial data privacy issues under General Data Protection Regulations;
 - The Company meets board diversity requirements under Nasdaq rules and Dutch law;
 - The Company's employees are 52% women and 48% men; and
 - Diversity is explicitly embedded in the Company's Core Values.

Despite not having a formal Diversity and Inclusion Policy, the Company does report on its gender diversity targets (see Chapter 5.8 – "Diversity").

5.2 Code of business conduct and ethics and other corporate governance practices

The Company has adopted a code of business conduct and ethics which can be accessed at <https://ir.pharvaris.com/corporate-governance/governance-documents>. The Company does not voluntarily apply other formal codes of conduct or corporate governance practices.

5.3 Risk management and control systems

See chapter 4.1 of this report for an overview of the main characteristics of the Company's risk management and control systems relating to the process of financial reporting by the Company and the Company's group companies whose financial information is included in the Consolidated Financial Statements.

5.4 General Meeting

5.4.1 Functioning of the General Meeting

Annually, at least one general meeting of the Company (the "**General Meeting**") must be held. This annual General Meeting must be held within six months after the end of the Company's fiscal year. A General Meeting must also be held within three months after the Board has decided that it is likely that the Company's equity has decreased to or below 50% of its paid up and called up share capital. In addition, without prejudice to the best practice provisions of the DCGC with respect to invoking a 'response period' or the provisions under Dutch law with respect to invoking a 'cooling-off period', a General Meeting must be held when requested by one or more shareholders and/or others with meeting rights under Dutch law collectively representing at least 10% of the Company's issued share capital, provided that certain criteria are met. Any additional General Meeting shall be convened whenever the Board would so decide. Each General Meeting must be held in Amsterdam, Arnhem, Assen, The Hague, Haarlem, 's-Hertogenbosch, Groningen, Leeuwarden, Lelystad, Leiden, Maastricht, Middelburg, Rotterdam, Schiphol (Haarlemmermeer), Utrecht or Zwolle. 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.

For purposes of determining who have voting rights and/or meeting rights under Dutch law at a General Meeting, the Board may set a record date. The record date, if set, shall be the 28th day prior to that of the General Meeting. Those who have voting rights and/or meeting rights under Dutch law on the record date and are recorded as such in one or more registers designated by the Board shall be considered to have those rights at the General Meeting, irrespective of any changes in the composition of the shareholder base between the record date and the date of the General Meeting. The Company's articles of association require shareholders and others with meeting rights under Dutch law to notify the Company of their identity and their intention to attend the General Meeting. This notice must be received by the Company ultimately on the seventh day prior to the General Meeting, unless indicated otherwise when such General Meeting is convened.

5.4.2 Powers of the General Meeting

All powers that do not vest in the Board pursuant to applicable law, the Company's articles of association or otherwise, vest in the General Meeting. The main powers of the General Meeting include, subject in each case to the applicable provisions in the Company's articles of association:

- a) the appointment, suspension and dismissal of Directors;
- b) the approval of certain resolutions of the Board concerning a material change to the identity or the character of the Company or its business;
- c) the reduction of the Company's issued share capital through a decrease of the nominal value, or cancellation, of shares in its capital;
- d) the adoption of the Company's statutory annual accounts;
- e) the appointment of the Dutch independent auditor to examine the Company's statutory annual accounts;
- f) amendments to the Company's articles of association;
- g) approving a merger or demerger by the Company, without prejudice to the authority of the Board to resolve on certain types of mergers and demergers if certain requirements are met; and
- h) the dissolution of the Company.

In addition, the General Meeting has the right, and the Board must provide, any information reasonably requested by the General Meeting, unless this would be contrary to an overriding interest of the Company.

5.4.3 Shareholder rights

Each share in the Company's capital carries one vote. Shareholders, irrespective of whether or not they have voting rights, have meeting rights under Dutch law (including the right to attend and address the General Meeting, subject to the concept of a record date as described in chapter 5.4.1). Furthermore, each share in the Company's capital carries an entitlement to dividends and other distributions as set forth in the Company's articles of association. Pursuant to the Company's articles of association, any such dividend or other distribution shall be payable on such date as determined by the Board and the Board may also set a record date for determining who are entitled to receive any such dividend or other distribution (irrespective of subsequent changes in the shareholder base). The record date for dividends and other distributions shall not be earlier than the date on which the dividend or other distribution is announced. In addition, shareholders have those rights awarded to them by applicable law.

5.5 Board

The Board is charged with managing the Company's affairs, which includes setting the Company's policies and strategy. Our executive director is charged primarily with the Company's day-to-day business and operations and the implementation of the Company's strategy. Our non-executive directors are charged primarily with the supervision of the performance of the duties of the Board. Each director is charged with all tasks and duties of the Board that are not delegated to one or more other specific directors by virtue of Dutch law, the Company's articles of association or any arrangement catered for therein (e.g., the internal rules of the Board). In performing their duties, our directors shall be guided by the interests of the Company and of the business connected with it.

As at December 31, 2023, the Board was composed as follows, which are all current directors on the Board of the date of this report:

Name and age	Gender identity	Nationality	Date of initial appointment	Expiration of current term of office	Attendance rate at meetings of the board
Berndt Modig (65) *	M	Swedish	September 30, 2015	At the end of the AGM to be held in 2024	89%
Hans Schikan (64) **	M	Dutch	August 28, 2019	At the end of the AGM to be held in 2024	89 %
David Meeker (68) **	M	American	January 1, 2021	At the end of the AGM to be held in 2025	100 %
Robert Glassman (62) **	M	American	January 1, 2021	At the end of the AGM to be held in 2025	100%
Viviane Monges (59) **	F	French	June 29, 2021	At the end of the AGM to be held in 2025	89 %
Elisabeth Björk (62) **	F	Swedish	December 1, 2021	At the end of the AGM to be held in 2026	100 %

* Executive director

** Non-executive director

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, Fontainebleau, 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.

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 a Board Member of Vicore Pharma (STO: VICO) and Organon Benelux and is Chairman of the Board of Microbiotica and Complix. 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 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, Portage Biotech and Jubilant.

87 [Table of Contents](#)

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 the Senior Vice President, Head of 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, Chalmers Ventures AB, Björks Matematik o Mera AB, rfidcompare europe AB, and Calliditas.

Viviane Monges

Ms. Monges has been a director since July 2021 and serves as the Chair of the Audit Committee. She currently also serves as Chair of the Board of Directors of Euroapi and is a Board member of Ferring Pharmaceuticals. She also serves as a non-executive director at ADC Therapeutics, and Novo Holdings. Prior to these roles, Ms. Monges 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.

5.6 Committees

5.6.1 General

The Board has established an audit committee, a compensation committee and a nomination and corporate governance committee. Each committee operates pursuant to its charter.

As at December 31, 2023, the committees were composed as follows:

Name	Audit committee (and attendance rate)	Compensation committee (and attendance rate)	Nomination and corporate governance committee (and attendance rate)
Elisabeth Björk, M.D.			X (100% attendance)
Robert Glassman M.D.	X (100% attendance)	X (100% attendance)	
David Meeker, M.D.		X (100% attendance)	X* (100% attendance)
Viviane Monges	X* (100% attendance)		
Hans Schikan, Pharm.D.	X (100% attendance)	X* (100% attendance)	

* Chairperson

5.6.2 Audit Committee

The responsibilities of our audit committee include:

- monitoring the Board with respect to (i) the relations with, and the compliance with recommendations and follow-up of comments made by, the Company's internal audit function and the Dutch independent auditor, and, if relevant, other external parties involved in the audit of the Company's sustainability reporting (ii) the Company's funding, (iii) the application of information and communication technology by the Company, including risks relating to cybersecurity and (iv) the Company's tax policy;
- the Company's compliance with applicable legal and regulatory requirements;
- the operation of the Company's code of business conduct and ethics and its other internal policies;

88 Table of Contents

- d) issuing recommendations concerning the appointment and the dismissal of the head of the Company's internal audit function and reviewing and discussing the performance of the Company's internal audit function;
- e) reviewing and discussing the Company's audit plan with the Company's internal audit function and the Dutch independent auditor;
- f) reviewing and discussing the audit results with the Company's internal audit function and the Dutch independent auditor, including (i) flaws in the effectiveness of the Company's internal risk management and control systems, (ii) findings and observations with a material impact on the Company's risk profile and (iii) failing in the follow-up of recommendations made previously by the Company's internal audit function;
- g) reviewing and discussing with the Dutch independent auditor, at least annually, (i) the scope and materiality of the Company's audit plan and the principal risks of the Company's annual financial reporting identified in such audit plan, (ii) the findings and outcome of the Dutch independent auditor of the Company's financial statements and its management letter and (iii) significant findings from the audit of the Company's financial statements and any problems or difficulties encountered, including restrictions on the scope of the Dutch independent auditor's activities or on access to requested information, as well as significant disagreements with the Company's management;
- h) receiving from the Dutch independent auditor a formal written statement at least annually delineating all relationships between the Dutch independent auditor and the Company consistent with applicable requirements of the Public Company Accounting Oversight Board regarding the Dutch independent auditor's communications with the audit committee concerning independence;
- i) determining whether and, if so, how the Dutch independent auditor should be involved in the content and publication of financial reports other than the Company's financial statements;
- j) resolving disagreements between the Company's management and the Dutch independent auditor regarding the Company's financial reporting;
- k) reviewing and discussing with the Dutch independent auditor any audit problems or difficulties and the response of the Company's management thereto, including those matters required to be discussed with the audit committee by the Dutch independent auditor pursuant to established auditing standards, including (i) restrictions on the scope of the Dutch independent auditor's activities or on access to requested information, (ii) accounting adjustments that were noted or proposed by the Dutch independent auditor but were "passed" as immaterial or otherwise, (iii) communications between the audit team and the audit firm's national office regarding auditing or accounting issues presented by the engagement, and (iv) management or internal control letters issued, or proposed to be issued, by the Dutch independent auditor;
- l) reviewing and discussing the effectiveness of the design and operation of the Company's risk management and control systems with the Board, the CEO and the CFO, including (i) identified material failings, deficiencies or material weaknesses in the Company's internal risk management and control systems, including whether there are significant deficiencies and material weaknesses in the design or operation of the Company's internal risk management and control systems which are reasonably likely to affect the Company's ability to record, process, summarize and report financial information and fraud involving the Company's management or other employees with a significant role in the design or operation of the Company's internal risk management and control systems and (ii) material changes made to, and material improvements planned for, the Company's internal risk management and control systems;
- m) assisting the Company in preparing the disclosure to be included in the Company's applicable filings as required by the Securities Act, the Exchange Act and their related rules;
- n) advising the Board regarding the Dutch independent auditor's nomination for (re)appointment or dismissal (including confirmation and evaluation on the rotation of the audit partners on the audit engagement team as required by applicable law and NASDAQ requirements) and preparing the selection of the Dutch independent auditor for such purpose, as relevant;
- o) reviewing and discussing the terms of engagement of the Dutch independent auditor to audit the Company's financial statements, to prepare or issue an audit report, or to perform other audit, review or attest services, submitting proposals to the Board concerning the Dutch independent auditor 's engagement to audit the Company's financial statements, in each case including the scope of the audit, the materiality standard to be applied and the Dutch independent auditor 's compensation and causing the Company, without further action, to pay the compensation of the Dutch independent auditor as approved by the audit committee;
- p) engagement of such independent legal, accounting and other advisors as the audit committee deems necessary or appropriate to carry out its responsibilities, including causing the Company, without further action, to pay the reasonable compensation of such advisors as approved by the audit committee;
- q) causing the Company to pay, without further action, the ordinary administrative expenses of the audit committee that are necessary or appropriate in carrying out its responsibilities;
- r) preparing the audit committee report that the SEC rules require to be included in the Company's annual proxy statement (if and when the Company would become subject to those rules);
- s) establishing policies for the Company's hiring of current or former employees of the Dutch independent auditor;
- t) establishing procedures for (i) the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and (ii) the confidential, anonymous submission by employees of the Company of concerns regarding questionable accounting or auditing matters;

89 [Table of Contents](#)

- u) reviewing potential conflicts of interest involving our directors, including whether they may take part in the deliberations and the decision-making on any issue as to which there may be a conflict;
- v) reviewing, approving and overseeing any transaction between the Company and any related persons on an ongoing basis, in accordance with the Company's policies and procedures; and
- w) developing and recommending to the Board the Company's related person transaction policy.

During the fiscal year to which this report relates, our audit committee met four times in order to carry out its responsibilities. The main items discussed at those meetings included the internal control remediation plan and follow-up on this during 2023, the (interim) financial statements, the actual financial results of each of the quarters, securities filings and financial press releases as well as the audit approach and the budget for 2023 and partly 2023.

5.6.3 Compensation committee

The responsibilities of our compensation committee include:

- a) reviewing and evaluating the Company's compensation policy (the "**Compensation Policy**") and benefits policies generally, including the review and recommendation of incentive-compensation and equity-based plans of the Company, as well as the compensation of the CEO and the Company's other executive officers;
- b) evaluate at least annually the CEO's performance in light of those goals and objectives, and make recommendations to the Board regarding the CEO's compensation level based on this evaluation;
- c) submitting proposals to the Board concerning changes to Compensation Policy, as relevant;
- d) submitting proposals to the Board concerning the compensation of the Company's executive officers and the individual directors, at least covering (i) the compensation structure, (ii) the amount of the fixed and variable compensation components, (iii) the applicable performance criteria (iv) the scenario analyses that have been carried out (v) the pay ratios within the Company's group, (vi) if it concerns the compensation of a director, the views of the director concerned with regard to the amount and structure of his own compensation and (vii) if considered appropriate by the Board or the compensation committee, the views of the executive officer concerned with regard to the amount and structure of his own compensation;
- e) the review and assessment of risks arising from the Compensation Policy and practices and whether any such risks are reasonably likely to have a material adverse effect on the Company;
- f) the preparation of the Company's compensation report for the Board;
- g) set the composition of the peer company group used for market comparison for executive compensation;
- h) the preparation of the compensation committee's report required by SEC rules or the rules of any other regulatory body; and
- i) the retention of or obtaining advice from a compensation consultant, legal counsel or other advisor as the compensation committee deems necessary or appropriate to carry out its responsibilities, including the appointment of such consultant, counsel or advisor and the ability to cause the Company, without further action, to pay with Company funds the reasonable compensation of such consultant, counsel or advisor as approved by the compensation committee, provided, however, that (i) in retaining or obtaining the advice of such consultant, counsel or advisor, other than in-house legal counsel, the compensation committee shall take into consideration the factors affecting independence and conflicts of interest required by applicable SEC rules and NASDAQ rules and (ii) the compensation committee will be responsible for the oversight of the work of any such consultant, counsel or advisor.

During the fiscal year to which this report relates, our compensation committee met four times in order to carry out its responsibilities. The main items discussed at those meetings included the performance and terms and conditions of our executive compensation, the long-term incentive grants analysis and recommendations and the non-executive salary increase and bonus proposal.

5.6.4 Nomination and corporate governance committee

The responsibilities of our nomination and corporate governance committee include:

- a) drawing up selection criteria and appointment procedures for our directors;
- b) reviewing the size and composition of the Board and submitting proposals for the composition profile of the Board;
- c) making recommendations to the Board as to the determination of independence of non-executive directors;
- d) reviewing the functioning of individual directors and reporting on such review to the Board; drawing up a plan for the succession of our directors;

90 [Table of Contents](#)

- e) submitting proposals for (re)appointment of our directors;
- f) supervising the policy of the Board regarding the selection criteria and appointment procedures for the Company's senior management;
- g) overseeing the self-evaluation of the Board and its committees to determine whether they are functioning effectively;
- h) reviewing and discussing with management disclosure of the Company's corporate governance practices, including information regarding the operations of the corporate governance committee and other Board committees, director independence and the director nominations process, and to recommend that this disclosure be included in the Company's annual report on Form 20-F;
- i) developing and implementing the goals the Company may establish from time to time with respect to its environmental, social and governance and sustainability matters, and provide guidance to the Board on such matters; and
- j) developing the Company's code of conduct, corporate governance guidelines and other corporate governance policies, including, at least annually, reviewing and reassessing the adequacy of the Company's code of conduct and recommending any proposed changes to the Board.

During the fiscal year to which this report relates, our nomination and corporate governance committee met four times in order to carry out its responsibilities. The main items discussed at those meetings included a regulatory update and committee governance.

5.7 Evaluation

During the fiscal year to which this report relates, the Board has evaluated its own functioning, the functioning of the committees of the Board and that of the individual directors on the basis of a questionnaire approved by the Nominating and Governance committee. The Company's Chief Legal Officer conducted interviews with each member of the Board utilizing the approved questionnaire. As part of these evaluations, the Board has considered (i) substantive aspects, mutual interaction, (ii) events that occurred in practice from which lessons may be learned and (iii) the desired profile, composition, competencies and expertise of the Board. These evaluations are intended to facilitate an examination and discussion by the Board of its effectiveness and areas for improvement. The Board conducted a self-evaluation in 2023 and reviewed the findings at the Company's September Board meeting. The overall assessment from the Board members is that the Board is performing well, has constructive discussions and is effective in its decision-making. The Board questionnaire addressed seven themes:

- Overall assessment and key priorities
- Board dynamics
- Board composition and succession planning
- Committee effectiveness and succession
- Relationship with CEO and executive management
- Board meetings
- Board evaluation outcome

On the basis of these evaluations, the Board has concluded that the Board is functioning properly.

5.8 Diversity

Diversity Policy. The Company does not have a Diversity and Inclusion Policy that is fully responsive to the DCGC; however, the Company has diversity objectives with respect to the composition of the Board as part of the Company's policy regarding the qualification and nomination of director candidates. The Company is committed to supporting, valuing and leveraging diversity and the Company recognizes and welcomes diversity with respect to gender, age, race, ethnicity, nationality, sexual orientation and other important cultural differences. In its evaluation of new candidates, the nominating and governance committee may consider race or ethnicity, nationality, gender, sexual orientation, age, background, education skills and experience, as well as the restrictions, requirements and recommendations concerning those matters under applicable law, Nasdaq rules or best practice provisions of the Dutch Corporate Governance Code in relation to the full Board and/or individual directors or director candidates. However, the Company also believes that there is a fine line between diversity and unintentional discrimination. For that reason, the importance of diversity, in and of itself, should not set aside the overriding principle that someone should be recommended, nominated and appointed for being "the right person for the job."

Although the Company has not yet set specific targets with respect to certain elements of diversity, the Company believes that it is important for the Board and its senior management to represent a diverse composite mix of personal backgrounds, experiences, qualifications, knowledge, abilities and viewpoints, consistent with the principles outlined above. The Company also seeks to combine the skills and experience of long-standing members of the Board and its senior management with the fresh perspectives, insights, skills and

91 [Table of Contents](#)

experiences of new candidates from time to time. To further increase the range of viewpoints, perspectives, talents and experience, the Company strives for a mix of ages among the Board and its senior management, but also does not set a specific target in this respect.

Diversity Targets. As of December 31, 2023, 4 out of 6 of the Directors were male and 2 out of 6 of the Directors were female. To the extent possible and practicable, the Company intends for the composition of the Board to remain as balanced as reasonably possible, provided for a minimum target of at least 30% of the directors to be male and at least 30% of them to be female.

The Company believes that the current composition of its Board has achieved the Company's diversity objectives, as outlined above, including the Company's diversity objective with respect to gender.

In connection with the operation of the Company's diversity objectives, the Company has defined its senior management. The Company's senior management consists of senior professionals holding an Officer role at Pharvaris, overseeing a department and relevant department budget and reporting to the CEO or being the CEO. As of December 31, 2023, 4 out of 9 senior management members were male and 5 out of 9 senior management members were female. To the extent reasonable and practicable, the Company intends for the composition of senior management to be at least 30% female. Based on the size of our senior management, the Company's goal is to maintain our current level of gender diversity and believes that the current composition of its senior management has more than achieved the Company's diversity objective with respect to gender.

The Company employs 81 persons as of December 31, 2023, of which 39 are male and 42 are female. The Company targets an overall gender ratio among its employees of at least 30% male employees and at least 30% female employees.

The Company has taken the following activities and measures for a more balanced gender ratio within the organization:

- establishing policies that support equal opportunities for employees, senior management and applicants for employment;
- encouraging and enforcing respectful communication and cooperation among all employees and senior management;
- fostering a corporate culture where employees and senior management are treated with dignity, respect and understanding;
- requiring employee and senior management participation in training on diversity and inclusion;
- actively encouraging employees and officers who feel that they have been subjected to discrimination or harassment to report this to their supervisor or to the Company's human resources department; and
- regularly review our corporate policies to ensure equal treatment.

Given the gender ratios both in the Board as well as senior management, we are satisfied overall with our efforts towards improving gender diversity and we believe that our activities, training, mentoring and programs will continue to enhance the Company's diversity objectives.

5.9 Corporate values and code of business conduct and ethics

We recently revised our code of business conduct and ethics which covers a broad range of matters including the handling of conflicts of interest, compliance topics (including reporting concerns), and other corporate policies such as insider trading and equal opportunity and non-discrimination standards. We believe our code of business conduct and ethics is effective.

We have defined and communicated internally and externally our Corporate Values which underpin our overall Company Culture and reflect the organization's brand. The values act as a set of guiding principles and beliefs and help the workforce function together as a team and work towards a common goal.

6. Compensation

6.1 Compensation policy

Pursuant to Section 2:135(1) DCC, the General Meeting has adopted a Compensation Policy. The Compensation Policy is designed to contribute to the Company's strategy, long-term interests and sustainability by:

- i. attracting, retaining and motivating highly skilled individuals with the qualities, capabilities, profile and experience needed to support and promote the growth and sustainable success of the Company and its business;
- ii. driving strong business performance, promoting accountability and incentivising the achievement of short and long-term performance targets with the objective of furthering long-term value creation in a manner consistent with the Company's identity, mission and values;

92 [Table of Contents](#)

- iii. assuring that the interests of the Directors are closely aligned to those of the Company, its business and its stakeholders; and
- iv. ensuring overall market competitiveness of the Compensation Packages, while providing the Board sufficient flexibility to tailor the Company's compensation practices on a case-by-case basis, depending on the market conditions from time to time.

We believe that this approach and philosophy benefits the realisation of the Company's long-term objectives while keeping with the Company's risk profile.

6.2 Compensation of directors

See Note 20 (Related parties) to the consolidated financial statements for an overview of the implementation of the Compensation Policy in the fiscal year to which this report relates. In determining the level and structure of the compensation of the directors in the fiscal year to which this report relates relevant scenario analyses carried out in advance have been considered as follows: In October 2023, with the support of an independent and objective Compensation consultant, a review and update of the global peer group was completed to reflect the Company moving towards a late stage (Phase 3) development company. This updated peer group and relevant market data was used in assessing and proposing adjustments to the Company's cash compensation and pay philosophy, and considering our approach to cash adjustments and equity awards for 2024.

6.3 Pay ratio

The DCGC recommends that the Company provide a ratio comparing the total annual compensation of our executive director and that of a "representative reference group" determined by the Company. We have chosen to compare the cash compensation of our Chief Executive Officer to that of a median full-time permanent employee. Our methodology for producing this ratio excludes employees employed on a non-permanent basis. We have used the aggregate target cash compensation over the fiscal year concerned as a reference amount (i.e., excluding the value of equity incentive awards and other non-cash compensation components). To calculate the ratio, we have annualized the salaries of employees who had worked with us for less than a year as of December 31, 2023, and have calculated the salaries of employees on a part-time basis to reflect a full-time employment. Based on this methodology, the ratio between the total target cash compensation (Annual Base Salary and bonus target) of our Chief Executive Officer and a median full-time permanent employee for the fiscal year to which this report relates is 1 to 3.20 (rounded to the nearest integer). This CEO pay ratio has remained relatively stable in 2023 compared to the CEO pay ratio reported in our previous report for 2022 at 1 to 3.18 (2021: 1 to 2.77).

7. Related party transactions

For information on related party transactions, see Note 20 (Related parties) to the Consolidated Financial Statements.

Where applicable, best practice provisions 2.7.3, 2.7.4 and 2.7.5 of the DCGC have been observed with respect to the transactions referenced above in this chapter 7.

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, 2022 and 2021, payments to Charité CRO with respect to this service contract amounted to €0.5 million, €0.4 million and €608, respectively.

The Group engages two management entities for the purpose of providing key management services to the Group. These management entities are considered related parties, as they provide key management services and the key management personnel have key management functions within these entities. Certain key management personnel are also shareholders of the Company. The aggregate amount of expense recognized in the consolidated statements of loss and comprehensive loss related to these related parties were €1.1 million in 2023 (2022: €1.2 million, 2021: €1.1 million).

The aggregate amounts payable to the related parties were €1.4 million (2022: €1.2 million, 2021: €1.6 million).

8. Protective Measures

We have adopted several provisions that may have the effect of making a takeover of our Company more difficult or less attractive, including:

- a provision that our directors may only be removed at the general meeting by a two-thirds majority of votes cast representing more than half of our issued share capital if such removal is not proposed by our Board;

93 [Table of Contents](#)

- our directors being appointed on the basis of a binding nomination by our Board, which can only be overruled by the general meeting 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 (in which case the Board shall make a new nomination);
- a provision which allows the former chairman of our Board or our 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 brought to our shareholders for a vote upon a proposal 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 one 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 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 a response period has been previously invoked or (ii) if a shareholder holds at least 75% of our issued share capital as a consequence of a successful public bid.

In addition, 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 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 (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).

94 [Table of Contents](#)

FINANCIAL STATEMENTS

Consolidated Financial Statements

Consolidated Statement of Loss and Comprehensive Loss

	Note	Years ended December 31,		
		2023	2022	2021
		€	€	€
Research and development expenses	3	(65,575,030)	(57,375,574)	(35,789,166)
General and administrative expenses	4	(31,338,590)	(29,339,034)	(18,349,460)
Total operating expenses		(96,913,620)	(86,714,608)	(54,138,626)
Finance (expenses) income	6	(2,912,643)	11,061,138	11,477,964
Loss before income tax		(99,826,263)	(75,653,470)	(42,660,662)
Income tax expense	7	(1,048,805)	(679,087)	(70,117)
Net Loss		(100,875,068)	(76,332,557)	(42,730,779)
Other comprehensive (loss) / income				
<i>Items that may be reclassified to profit or loss:</i>				
Exchange gain (loss) arising on translation of foreign operations		(57,874)	17,362	30,293
Total comprehensive loss attributable to:				
Equity holders of the Company		(100,932,942)	(76,315,195)	(42,700,486)
Basic and diluted loss per share	19	(2.63)	(2.27)	(1.40)

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

Consolidated Statement of Financial Position

	Notes	As at December 31, 2023 €	As at December 31, 2022 €
Assets			
Non-current assets			
Property, plant and equipment	8	223,678	193,474
Right of use assets	9	231,893	432,965
Deferred tax assets	7	387,529	259,803
Current assets			
Current tax receivable	10	615,538	—
Receivables	10	423,486	382,468
Other current assets	11	5,580,704	4,626,844
Cash and cash equivalents	12	391,231,637	161,837,429
Total assets		<u>398,694,465</u>	<u>167,732,983</u>
Equity and liabilities			
Equity			
	13		
Share capital		6,274,833	4,057,976
Share premium		615,811,986	289,177,197
Other reserves		27,894,796	20,169,459
Currency translation reserve		(14,584)	43,290
Accumulated loss		(265,918,628)	(164,188,892)
Total equity		<u>384,048,403</u>	<u>149,259,030</u>
Long term liabilities			
Non-current lease liability	9	43,564	249,418
Current liabilities			
Trade and other payables	14	2,909,725	6,685,080
Accrued liabilities	16	11,067,510	10,890,749
Current lease liability	9	195,341	187,404
Current tax payable		429,922	461,302
Total liabilities		<u>14,646,062</u>	<u>18,473,953</u>
Total equity and liabilities		<u>398,694,465</u>	<u>167,732,983</u>

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, 2021		235,693	138,034,580	1,979,875	(4,365)	(44,459,954)	95,785,829
Net Loss		—	—	—	—	(42,730,779)	(42,730,779)
Increase in par value		2,592,621	(2,592,621)	—	—	—	—
Issue of share capital	13	1,141,329	156,014,570	—	—	—	157,155,899
Transaction costs on issue of shares		—	(13,154,360)	—	—	—	(13,154,360)
Currency translation reserve		—	—	—	30,293	—	30,293
Settlement of share-based payments	18	8,584	440,731	(401,846)	—	(377,668)	(330,199)
Share-based payments	18	—	—	8,196,387	—	—	8,196,387
Balance at December 31, 2021		<u>3,978,227</u>	<u>278,742,900</u>	<u>9,774,416</u>	<u>25,928</u>	<u>(87,568,401)</u>	<u>204,953,070</u>
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		<u>4,057,976</u>	<u>289,177,197</u>	<u>20,169,459</u>	<u>43,290</u>	<u>(164,188,892)</u>	<u>149,259,030</u>
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)
Increase in par value		—	—	—	—	—	—
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		<u>6,274,833</u>	<u>615,811,986</u>	<u>27,894,796</u>	<u>(14,584)</u>	<u>(265,918,628)</u>	<u>384,048,403</u>

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

Consolidated Statement of Cash Flows

	Notes	Years ended December 31,		
		2023	2022	2021
		€	€	€
Operating activities				
Loss before tax		(99,826,263)	(75,653,470)	(42,660,662)
<i>Non-cash adjustments to reconcile loss before tax to net cash flows / used in operations:</i>				
Share-based payment expense	5	10,663,226	11,349,200	8,196,387
Depreciation expense	8 & 9	257,551	152,941	77,370
Net foreign exchange (gain) loss		2,794,435	(11,100,392)	(11,760,469)
Finance (income) costs		(204,019)	39,254	267,700
<i>Changes in working capital:</i>				
Decrease (increase) in receivables		(41,051)	317,612	(130,501)
Decrease (increase) in other current assets		(953,861)	(2,511,076)	239,875
(Decrease) increase in trade and other payables		(4,171,990)	3,905,486	1,662,686
Increase (decrease) in accrued liabilities		(695,753)	6,664,878	(196,755)
Income taxes paid		(1,108,410)	(182,824)	(27,615)
Received (paid) interest		237,042	(144,243)	(267,700)
Net cash flows used in operating activities		(93,049,093)	(67,162,634)	(44,599,684)
Investing activities				
Purchase of property, plant and equipment	8	(89,984)	(124,296)	(130,032)
Net cash flows used in investing activities		(89,984)	(124,296)	(130,032)
Financing activities				
Proceeds from issue of shares and pre-funded warrants	13	342,911,317	9,609,865	156,825,699
Transaction costs		(17,297,810)	(839,970)	(13,154,360)
Payment of principal portion of lease liabilities		(220,507)	(119,527)	—
Net cash flows provided by financing activities		325,393,000	8,650,368	143,671,339
Net (decrease) increase in cash and cash equivalents		232,253,923	(58,636,562)	98,941,623
Cash and cash equivalents at the beginning of the year		161,837,429	209,353,132	98,628,871
Effect of exchange rate changes		(2,859,715)	11,120,859	11,782,638
Cash and cash equivalents at the end of the year	12	391,231,637	161,837,429	209,353,132

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, 2023 were authorized for issue in accordance with a resolution of the directors on May 30, 2024.

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 clinical-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	
			2023	2022
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 faces the market/external parties and makes all operational group 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 International Financial Reporting Standards as adopted by the European Union (IFRS-EU) and with Part 9 of Book 2 of the Dutch Civil Code.

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 Group's Chief Operating Decision Maker, 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

100 Table of Contents

whole. The Executive Committee is identified as the CODM and 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.

101 Table of Contents

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, 2023, 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.

102 [Table of Contents](#)

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.

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 2023 or 2022. 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 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

IFRS 17 Insurance Contracts

In May 2017, the IASB issued IFRS 17 Insurance Contracts, a comprehensive new accounting standard for insurance contracts covering recognition and measurement, presentation and disclosure. Once effective, IFRS 17 will replace IFRS 4 Insurance Contracts. In June 2020, the IASB issued amendments to IFRS 17. These amendments included changing the effective date to 2023. Effective for annual periods beginning on or after January 1, 2023. The amendments do not have a material impact on the Group.

Definition of Accounting Estimates - Amendments to IAS 8

In February 2021, the Board issued amendments to IAS 8, in which it introduces a new definition of 'accounting estimates'. The amendments clarify the distinction between changes in accounting estimates and changes in accounting policies and the correction of errors. Also, they clarify how entities use measurement techniques and inputs to develop accounting estimates. Effective for annual periods beginning on or after January 1, 2023. The amendments do not have a material impact on the Group.

Disclosure of Accounting Policies (Amendments to IAS 1 and IFRS Practice Statement 2)

The amendments require that an entity discloses its material accounting policies, instead of its significant accounting policies. Further amendments explain how an entity can identify a material accounting policy. Examples of when an accounting policy is likely to be material are added. To support the amendment, the Board has also developed guidance and examples to explain and demonstrate the application of the 'four-step materiality process' described in IFRS Practice Statement 2.

The amendments are effective for annual reporting periods beginning on or after January 1, 2023.

Deferred tax related to Assets and Liabilities arising from a single transaction

On May 7, 2021 the IASB issued Deferred Tax related to Assets and Liabilities arising from a Single Transaction (Amendments to IAS 12), which specifies how companies should account for deferred tax on transactions such as leases and decommissioning obligations as

104 [Table of Contents](#)

of initial recognition. The amendments clarify that the initial recognition exemption does not apply to transactions in which equal amounts of deductible and taxable temporary differences arise on initial recognition. Therefore, companies are required to recognize the deferred tax effects thereon to the extent that the related assets or liabilities provide for offsetting temporary differences upon recognition date. The amendments are effective for annual reporting periods beginning on or after January 1, 2023, with early application permitted. The amendments do not have a material impact on the Group.

Amendments to IAS 1: Classification of Liabilities as Current or Non-current

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.

International Tax Reform — Pillar Two Model Rules (Amendments to IAS 12)

In May 2023, the International Accounting Standards Board (the IASB or Board) issued International Tax Reform—Pillar Two Model Rules – Amendments to IAS 12 (the Amendments) to clarify the application of IAS 12 Income Taxes to income taxes arising from tax law enacted or substantively enacted to implement the Organisation for Economic Co-operation and Development (OECD)/G20 Inclusive Framework on Base Erosion and Profit Shifting (BEPS) Pillar Two model rules (Pillar Two) income taxes. The application of the exception to recognize deferred tax balances with regard to Pillar Two rules and disclosure of that fact is effective immediately, the other disclosure requirements are effective for annual reporting periods beginning on or after 1 January 2023, but not required in any interim financial statements for 2023. 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.

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 are not expected to 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 are not expected to have a material impact on 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

105 [Table of Contents](#)

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

	2023	2022	2021
	€	€	€
Personnel expenses (Note 5)	(19,132,307)	(13,334,350)	(7,988,096)
Clinical expenses	(30,690,293)	(27,653,658)	(16,944,557)
Nonclinical expenses	(8,977,187)	(4,853,822)	(3,891,479)
Manufacturing costs	(6,500,986)	(11,181,355)	(6,325,068)
License costs	—	—	(500,000)
Intellectual Property costs	(274,257)	(352,389)	(139,966)
	<u>(65,575,030)</u>	<u>(57,375,574)</u>	<u>(35,789,166)</u>

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.

Nonclinical expenses include costs of our outsourced discovery, preclinical and nonclinical development studies.

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.

License costs consist of a milestone payment of €0.5 million during 2021, which was paid to AnalytiCon upon commencement of Phase 2 development.

4. General and administrative expenses

	2023	2022	2021
	€	€	€
Personnel expenses (Note 5)	(13,314,359)	(13,484,996)	(7,033,913)
Consulting fees	(602,110)	(898,435)	(757,233)
Professional fees	(4,689,462)	(3,972,771)	(2,868,684)
Accounting, tax and auditing fees	(2,029,554)	(1,652,995)	(1,306,714)
Insurance, facilities and office expenses	(6,031,513)	(6,443,709)	(5,648,763)
Travel expenses	(1,797,588)	(1,105,961)	(143,582)
Other expenses	(2,874,004)	(1,780,167)	(590,571)
	<u>(31,338,590)</u>	<u>(29,339,034)</u>	<u>(18,349,460)</u>

In 2022 and 2021 the Group entered into a number of short-term rental arrangements, the expenses are included in "Other expenses".

106 Table of Contents

Depreciation expense of €0.06 million (2022: €0.04 million; 2021: €0.08 million), which relate to property, plant and equipment and leases and is included in the 'Other expenses' line.

5. Personnel expenses

	2023	2022	2021
	€	€	€
Wages and salaries	(18,746,645)	(13,408,411)	(6,080,098)
Pension charges	(1,156,028)	(803,460)	(251,667)
Other social security charges	(1,880,767)	(1,258,275)	(493,857)
Share-based payments	(10,663,226)	(11,349,200)	(8,196,387)
	<u>(32,446,666)</u>	<u>(26,819,346)</u>	<u>(15,022,010)</u>

The number of staff (in FTEs) employed by the Group at December 31, 2023 was 82 (2022: 65; 2021: 34).

6. Finance income

	2023	2022	2021
	€	€	€
Foreign exchange differences	(3,116,662)	11,100,392	11,760,469
Interest income (expense)	224,494	(16,105)	(267,510)
Other finance expenses	(20,475)	(23,149)	(14,995)
	<u>(2,912,643)</u>	<u>11,061,138</u>	<u>11,477,964</u>

Other finance expenses are mainly related to bank charges.

7. Income taxes

	2023	2022	2021
	€	€	€
Current income tax expense	(473,623)	(757,413)	(131,921)
Deferred tax (charge) benefit	(575,182)	78,326	61,804
Income tax benefit / (expense)	<u>(1,048,805)</u>	<u>(679,087)</u>	<u>(70,117)</u>

The current tax expenses for the years ended December 31, 2023, 2022 and 2021 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 December 31, 2021 it is fully related to the Company's U.S. subsidiary. For the year ended December 31, 2023, a tax benefit of €0.7 million is additionally directly recognized in equity (2022: €0.3 million; 2021: €Nil)

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:

	2023	2022	2021
	€	€	€
Loss before income tax	(99,826,263)	(75,653,470)	(42,660,662)
Income tax at statutory income tax rate in The Netherlands (2023: 25.8%; 2022 & 2021: 25%)	25,755,176	19,518,595	10,665,166
Effect of tax rates in other countries	(14,334,369)	(10,823,383)	(7,482,832)
Derecognition of previously unrecognized deferred tax assets	(58,506)	(554,853)	—
Current period losses for which no deferred tax asset has been recognized	(14,771,877)	(9,184,919)	(2,910,890)
Nondeductible expenses	(458,482)	383,153	(353,543)
Prior period adjustments	2,819,253	(17,680)	11,982
Income tax benefit / (expense)	<u>(1,048,805)</u>	<u>(679,087)</u>	<u>(70,117)</u>

The effective tax rate for 2023 is (1.1)% (2022: (0.9)%; 2021: (0.2)%).

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 and in the Netherlands.

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 and the utilization of the previously unrecognized losses carry forward losses of the Dutch fiscal unity that are lower than estimated in the previous year. The Company did not recognize the tax benefit of the losses incurred in previous years.

The Group has tax loss carry-forwards as of December 31, 2023 of approximately €325.0 million (2022: €182.3 million; 2021: €95.7 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
2027	—	—	—
2028	103,332,348	—	103,332,348
2029	87,214,172	—	87,214,172
2030	103,751,019	—	103,751,019
Unlimited	—	30,737,684	30,737,684
Total carry-forward losses	294,297,539	30,737,684	325,035,223

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 €0.4 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, 2023	1,792,382	—	301,852	2,094,234
(Charged)/credited				
- Comprehensive (loss) income	(37,609)	—	111,064	73,455
- Currency translation differences	—	—	(12,716)	(12,716)
At December 31, 2023	<u>1,754,773</u>	<u>—</u>	<u>400,200</u>	<u>2,154,973</u>
Deferred tax liability				
At January 1, 2023	—	(42,048)	(1,792,383)	(1,834,431)
(Charged)/credited				
- Comprehensive income (loss)	—	28,489	37,610	66,099
- Currency translation differences	—	888	—	888
At December 31, 2023	<u>—</u>	<u>(12,671)</u>	<u>(1,754,773)</u>	<u>(1,767,444)</u>
Net deferred tax assets at December 31, 2023				<u>387,529</u>

	R&D expenses	Fixed assets	Non-current provisions and liabilities	Total
	€	€	€	
Deferred tax assets				
At January 1, 2022	1,909,916	—	238,508	2,148,424
(Charged)/credited				
- Profit or loss	(117,534)	—	49,354	(68,180)
- Currency translation differences	—	—	13,990	13,990
At December 31, 2022	<u>1,792,382</u>	<u>—</u>	<u>301,852</u>	<u>2,094,234</u>
Deferred tax liability				
At January 1, 2022	—	(66,456)	(1,909,916)	(1,976,372)
(Charged)/credited				
- Profit or loss	—	28,972	117,533	146,505
- Currency translation differences	—	(4,564)	—	(4,564)
At December 31, 2022	<u>—</u>	<u>(42,048)</u>	<u>(1,792,383)</u>	<u>(1,834,431)</u>
Net deferred tax assets at December 31, 2022				<u>259,803</u>

The total unrecognized deferred tax assets from temporary differences amounts to €11.0 million for the year ended December 31, 2023, (2022: €8.7 million; 2021: €23.8 million).

8. Property, plant and equipment

	Notes	2023	2022
		€	€
Net book value			
As of January 1,		193,474	108,098
Additions		90,051	124,296
Depreciation expenses	4	(59,847)	(38,920)
As of December 31,		<u>223,678</u>	<u>193,474</u>
Cumulative depreciation			
As of January 1,		(65,526)	(26,606)
Depreciation		(59,847)	(38,920)
As of December 31,		<u>(125,373)</u>	<u>(65,526)</u>
Cumulative Costs			
As of January 1,		259,000	134,704
Additions		90,051	124,296
As of December 31,		<u>349,051</u>	<u>259,000</u>

During 2023, the Group acquired assets with a cost of €0.09 million (2022: €0.1 million; 2021: €0.08 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:

	2023	2022
	€	€
As of January 1,	432,965	243,251
(Disposals) / Additions	(3,302)	303,734
Depreciation charges	(197,770)	(114,020)
As of December 31,	<u>231,893</u>	<u>432,965</u>

The following table provides information about the Group's lease liabilities at December 31, 2023:

	2023	2022
	€	€
Office leases	(238,905)	(436,822)
Total lease liability	(238,905)	(436,822)
Current Portion	(195,341)	(187,404)
Non-current Portion	(43,564)	(249,418)

The following table provides information about the maturities of the Company's lease liabilities at December 31, 2023:

Years ending December 31,	Operating Leases	
2024	158,458	
2025	96,250	
2026	-	
Thereafter	-	
Total lease payments	254,708	
Less: imputed interest	15,803	
Total lease liabilities	<u>238,905</u>	
Current lease liabilities	195,341	
Long-term lease liabilities	<u>43,564</u>	

Office leases consists of a lease agreement entered into on June 1, 2021 for office space in Lexington, United States of America, or the U.S., and a lease entered into on December 1, 2022, for offices in Leiden, The Netherlands. Both leases have lease terms of three years and were assessed as being long-term.

The average incremental borrowing rate applied to the lease liabilities was 7.77% during the twelve months ended December 31, 2023 and 2022. Depreciation expense of €0.2 million, €0.1 million and €0.1 million for the for the years ended December 31, 2023, 2022 and 2021, 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 2023 was €0.2 million (2022: €0.3 million; 2021: €0.3 million) and is included in facility, communication, and office expenses

Cash outflows related to leases during the years ended December 31, 2023, 2022 and 2021 were €0.2 million, €0.1 million and €0.1 million, respectively.

10. Receivables

	2023	2022
	€	€
Current tax receivable	615,538	—
VAT receivables	423,486	382,468
	<u>1,039,024</u>	<u>382,468</u>

110 Table of Contents

11. Other current assets

	2023	2022
	€	€
Prepayments	4,959,889	4,044,255
Other assets	620,815	582,589
	<u>5,580,704</u>	<u>4,626,844</u>

Prepayments mainly relate to prepaid insurance, sign-on bonus to personnel, prepaid research and development expenses and rent.

Other assets per December 31, 2023 and 2022 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

	2023	2022
	€	€
Cash and cash equivalents	391,231,637	161,837,429
	<u>391,231,637</u>	<u>161,837,429</u>

The Cash and cash equivalents consist of bank balances and are not subject to any restriction. Of the cash on hand, €65,567 relates to guarantees.

13. Equity

On December 31, 2023, the Company's 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, 2023, the total number of issued and fully paid shares was 52,290,212 (2022: 33,816,459; 2021: 33,151,881). On December 31, 2023, the issued share capital totaled €6.3 million (2022: €4.1 million; 2021: €4.0 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.

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.

	2023	2022
	Number of shares	Number of shares
Ordinary shares	52,290,212	33,816,459
	52,290,212	33,816,459

No dividend was distributed in 2023, 2022 or 2021.

111 [Table of Contents](#)

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

	2023	2022
	€	€
Trade payables	2,909,725	5,979,168
Tax and social security liabilities	—	705,912
	<u>2,909,725</u>	<u>6,685,080</u>

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

	2023	2022
	€	€
Consulting, professional and audit liability	351,064	642,662
Clinical accrued liabilities	1,832,590	3,824,468
Manufacturing accrued liabilities	2,079,900	2,285,584
Nonclinical accrued liabilities	493,907	885,030
Personnel related accruals	5,892,087	2,971,068
Other accrued liabilities	417,962	281,937
	<u>11,067,510</u>	<u>10,890,749</u>

17. Financial risk management

The Group's principal financial instruments consist of cash and cash equivalents, receivables, 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. We received the proceeds from our financings in U.S. dollars. We seek to minimize our exchange rate risk in our cash positions by taking into considerations market conditions and keeping currencies in which we expect to incur the majority of our near future expenses and make related payments from those positions.

For the year ended December 31, 2023, the Group recognized a foreign exchange loss of €3.1 million and foreign exchange gains of €11.1 million and €11.8 million, for the years ended December 31, 2022 and 2021, respectively. The foreign exchange gain was primarily related to the U.S. dollar cash holding of its subsidiary and the associated strengthening of the U.S. dollar compared to euro during the year.

Material occurrences of foreign exchange losses would negatively affect the Group.

At December 31, 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 €18.8 million and €6.8 million higher / lower, respectively.

At December 31, 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 €7.1 million and €2.0 million higher / lower, respectively.

The Group keeps an amount of \$208.2 million, €131.8 million and CHF65.8 million in its bank accounts as of December 31, 2023.

112 [Table of Contents](#)

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 €391.2 million of cash on the balance sheet at December 31, 2023. 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, 2023 and 2022 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, 2023, 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, 2023, the Company has cash and cash equivalents of €391.2 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:

	<u>Less than 12 months</u>	<u>1 to 5 years</u>	<u>Total</u>
	€	€	€
December 31, 2023			
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
	<u>Less than 12 months</u>	<u>1 to 5 years</u>	<u>Total</u>
	€	€	€
December 31, 2022			
Trade and other payables	6,685,080	—	6,685,080
Accrued liabilities	10,890,749	—	10,890,749
Lease Liabilities	222,182	254,709	476,891

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, 2021 the Company granted a total of 107,000 stock options to members of key management with an exercise price of €7,25 per share with a final exercise date of December 31, 2030 unless forfeited or exercised on an earlier date.

113 [Table of Contents](#)

On February 4, 2021, a total of 873,000 stock options were granted to members of key management with an exercise price of \$20 per share with a final exercise date of February 3, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on the 12-month anniversary of the vesting commencement date, 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 25, 2021, the grant date fair value was determined for 88,000 stock options granted to a member of key management with an exercise price of €2.38 per share with a final exercise date of February 2, 2030 unless forfeited or exercised on an earlier date. Each month, 1/48 of the options will vest, with final vesting on February 4, 2024.

On June 25, 2021, a total of 14,000 stock options were granted to a member of key management with an exercise price of \$20 per share with a final exercise date of February 3, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on February 3, 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 July 1, 2021, a total of 150,000 stock options were granted to members of key management with an exercise price of \$17.43 per share with a final exercise date of June 30, 2031 unless forfeited or exercised on an earlier date. 25% of the aggregate number of share options shall vest on June 30, 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 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.

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, 2023, 2022 and 2021 that related to Options, amounted to €6.2 million, €7.6 million and €7.0 million, respectively.

The following table illustrates the number and weighted average exercise prices of, and movements in, stock options during the year:

	2023 Number stock options	Weighted average exercise price €	2022 Number stock options	Weighted average exercise price €	2021 Number stock options	Weighted average exercise price €
Outstanding January 1,	3,181,538	9.69	2,470,295	9.18	1,465,295	1.85
Granted	936,000	6.53	742,500	16.12	1,144,000	15.80
Exercised	(241,825)	1.45	(31,257)	2.38	(34,000)	2.38
Forfeited	(45,061)	8.90	—	—	(105,000)	16.67
Outstanding December 31,	3,830,652	9.46	3,181,538	9.69	2,470,295	9.18

114 Table of Contents

Out of the total outstanding stock options of 3,830,652 at December 31, 2023 (2022: 3,181,538, 2021: 2,470,295), 1,949,721 stock options were exercisable (2022: 1,585,404; 2021: 469,630). The options outstanding at December 31, 2023 had an exercise price in the range of €0.01 to €16.88 (2022: €0.01 to €16.78; 2021: €0.01 to €16.67) and a weighted-average remaining contractual life of 6.4 years (2022: 7.5 years; 2021: 8.0 years).

A total of 241,825 share options were exercised during the period ended December 31, 2023 (2022: 31,257; 2021: 34,000) and had a weighted-average share price of €20.08 (2022: €11.74; 2021: €38.75) at the date of exercise.

Restricted Award Agreements

In 2021 the Company granted a total of 175,991 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 2021 amounted to €17.0. The expenses are recognized over the service period in the consolidated statements of loss and comprehensive loss.

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. The expenses are recognized over the service period in the consolidated statements of loss and comprehensive loss.

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. The 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, 2023, 2022 and 2021 that related to RSUs, amounted to €4.5 million, €3.8 million and €1.2 million, respectively.

The following table illustrates the number of and movements in unvested RSUs during the year:

	<u>2023</u>	<u>2022</u>	<u>2021</u>
	Number RSUs	Number RSUs	Number RSUs
Outstanding January 1,	795,694	259,714	153,595
Granted	528,004	681,588	175,991
Vested and settled	(209,671)	(65,846)	(57,372)
Forfeited	(80,213)	(79,762)	(12,500)
Outstanding December 31,	<u>1,033,814</u>	<u>795,694</u>	<u>259,714</u>

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:

	<u>November 15, 2023</u>	<u>April 6, 2023</u>	<u>June 1, 2022</u>	<u>April 1, 2022</u>	<u>January 1, 2022</u>	<u>July 1, 2021</u>	<u>June 25, 2021</u>	<u>June 25, 2021</u>	<u>February 4, 2021</u>	<u>January 1, 2021</u>
							<u>Option 1</u>	<u>Option 2</u>		
Number of options	90,000	846,000	120,000	552,500	70,000	150,000	14,000	88,000	873,000	107,000
Fair value of the options (€)	€ 12.27	€ 5.92	€ 11.89	€ 11.50	€ 9.08	€ 10.50	€ 10.90	€ 13.73	€ 11.88	€ 5.06
Fair value of the ordinary shares (€)	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65	€ 14.67	€ 15.46	€ 15.46	€ 16.69	€ 7.25
Exercise price (€)	€ 15.12	€ 7.36	€ 16.88	€ 16.42	€ 12.65	€ 14.67	€ 16.74	€ 2.38	€ 16.69	€ 7.25
Expected volatility (%)	100%	100%	80%	80%	85%	85%	85%	85%	85%	85%
Expected life (years)	6.1	6.1	6.1	6.1	6.1	6.1	6.1	4.6	6.1	6.0
Risk-free interest rate (%)	4.6%	3.6%	3.0%	2.6%	1.4%	1.2%	1.2%	-0.5%	0.8%	-0.6%
Expected dividend yield	-	-	-	-	-	-	-	-	-	-

Expected volatility in 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 German government Strip bonds or 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.

On February 5, 2021, the Company's ordinary shares began trading on the Nasdaq Stock Exchange. From that date, the shares of the Company were traded at a regulated stock exchange. For the determination of the fair value on the grant date, the closing price on the grant date is used.

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.

Outstanding options are not included in the calculation of diluted earnings per share because they are antidilutive in 2023, 2022 and 2021.

Basic and diluted loss per share

	Year Ended December 31,		
	2023	2022	2021
	€	€	€
Net Loss	(100,875,068)	(76,332,557)	(42,700,486)
Weighted average number of ordinary shares outstanding	38,391,654	33,585,976	30,411,902
Basic and diluted loss per share	(2.63)	(2.27)	(1.40)

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, 2022 and 2021, payments to Charité CRO with respect to this service contract amounted to €0.5 million, €0.4 million and €608, respectively.

Key management personnel compensation

	2023	2022	2021
	€	€	€
Short term employee benefits	4,467,603	3,461,860	2,517,211
Post employee benefits	189,996	148,678	80,482
Share-based payments	6,252,492	6,524,726	6,269,218
Total	10,910,091	10,135,264	8,866,911

At the end of financial year 2020 an amount of €120,000 of short-term employee benefits was capitalized on the consolidated statements of financial position. This amount was recognized in the Group's statements of profit or loss and other comprehensive income in 2021. As at 31 December 2023 and 2022, no short-term employee benefits have been capitalized.

The Group engages two management entities for the purpose of providing key management services to the Group. These management entities are considered related parties, as they provide key management services and the key management personnel have key management functions within these entities. Certain key management personnel are also shareholders of the Company. The aggregate amount of expense recognized in the consolidated statements of loss and comprehensive loss related to these related parties were €1.1 million in 2023 (2022: €1.2 million, 2021: €1.1 million).

The aggregate amounts payable to the related parties were €1.4 million (2022: €1.2 million, 2021: €1.6 million).

The below table shows in euro the remuneration of the individual members of the Board of Directors for the year ended December 31, 2023 and 2022:

	Salary	Bonus	Pension and social securities	Management fee	Share-based compensation	Total remuneration 2023	Total remuneration 2022
	€	€	€	€	€	€	€
Mr. B. Modig	595,693	265,760	73,831	-	1,401,365	2,336,649	2,413,678
Mr. H. Schikan	-	-	-	56,450	139,404	195,854	269,146
Mr. D. Meeker	-	-	-	87,136	373,431	460,567	281,888
Mr. R. Glassman	-	-	-	45,072	198,914	243,986	195,605
Ms. V. Monges	-	-	-	57,106	201,729	258,835	309,621
Ms. E. Björk	-	-	-	41,591	255,859	297,450	318,576
Ms. A. de Jonge - Schuermans(1)	-	-	-	27,610	(60,807)	(33,197)	236,603

Share-based compensation represents the impact in the result of the Company for the expenses granted to the members of the Board of Directors.

	Number of options granted for the year ended December 31, 2023	Grant date / Expiry date	Exercise price	Number of options granted for the year ended December 31, 2022	Grant date / Expiry date	Exercise price
			\$			\$
Mr. B. Modig	170,000	April 6, 2023 April 6, 2033	8.05	140,000	April 1, 2022 April 1, 2032	18.14
Mr. D. Meeker	21,000	April 6, 2023 April 6, 2033	8.05	17,500	April 1, 2022 April 1, 2032	7.89
Ms. E. Björk	21,000	April 6, 2023 April 6, 2033	8.05	35,000	January 1, 2022 January 1, 2032	14.39
				17,500	April 1, 2022 April 1, 2032	18.14
Mr. H. Schikan	21,000	April 6, 2023 April 6, 2033	8.05	17,500	April 1, 2022 April 1, 2032	18.14
Mr. R. Glassman	21,000	April 6, 2023 April 6, 2033	8.05	17,500	April 1, 2022 April 1, 2032	18.14
Ms. V. Monges	21,000	April 6, 2023 April 6, 2033	8.05	17,500	April 1, 2022 April 1, 2032	18.14
Ms. De Jonge Schuermans	21,000	April 6, 2023 April 6, 2033	8.05	35,000	January 1, 2022 January 1, 2032	14.39

Regarding the vesting dates, 1/4th of the aggregate number of shares subject to the option shall vest on the 12-month anniversary of the applicable vesting commencement date and 1/48th of the aggregate number of shares subject to the option shall vest on each subsequent monthly anniversary of the applicable vesting commencement date until either the option is fully vested or the option-holder's continuous service terminates.

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.

Non-cancellable service contracts

The Group has entered into research and development commitments in relation to the developments of Group's oral bradykinin-B2-receptor antagonist.

118 [Table of Contents](#)

Commitment for the minimum payments in relation to the non-cancellable service contracts amount to €49 million as of December 31, 2023 (2022: €28 million), of which €44.8 million is committed in the year ending December 31, 2024.

On March 31, 2016, the Company entered into a license agreement (the “AnalytiCon License”) and a research agreement with AnalytiCon to collaborate for the development of an orally available bradykinin-B2-receptor antagonist. Pursuant to the AnalytiCon License, the Company acquired a worldwide, exclusive license from AnalytiCon 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, PHVS416 and PHVS719 are subject to the AnalytiCon License.

Under the AnalytiCon License, up to €10.5 million in aggregate potential milestone payments remain outstanding. In addition, the Company will be required to pay AnalytiCon 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 AnalytiCon 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

The Group had no contingent liabilities and no contingent assets at December 31, 2023 and 2022.

23. Events after the reporting period

On April 10, 2024, the Company announced the appointment of Mr. David W. Nassif to the newly created position of Chief Financial Officer, effective April 15, 2024. As Chief Financial Officer, Mr. Nassif will lead and oversee all of the Company’s financial activities and will be responsible for maintaining the financial health of the Company.

Joan Schmidt, our Chief Legal Officer, has announced that she will be leaving the Company effective June 1, 2024. David Nassif will assume oversight of the legal and compliance department and will act as the corporate secretary until a successor joins the Company.

Signatories to the financial statements

Leiden, May 30, 2024.

Pharvaris N.V.
Board of directors

/s/ D. Meeker
D. Meeker

/s/ E. Björk
E. Björk

/s/ V. Monges
V. Monges

/s/ R. Glassman
R. Glassman

/s/ B.A.E. Modig
B.A.E. Modig

/s/ J.G.C.P. Schikan
J.G.C.P. Schikan

[Table of Contents](#)

Company only Financial Statements

Statement of financial position

	Notes	As at December 31, 2023 €	As at December 31, 2022 €
Assets			
Non-current assets			
Financial Fixed Assets	1	361,132,187	134,683,240
Current assets			
Receivables	2	69,883	116,948
Prepayments, other receivables and deferred expenses	3	861,495	1,025,391
Cash and cash equivalents	4	22,203,896	14,556,660
Total assets		<u>384,267,461</u>	<u>150,382,239</u>
Equity and liabilities			
Equity			
Share capital	5	6,274,833	4,057,976
Share premium		615,811,986	289,177,197
Other reserves		27,894,796	20,169,459
Legal reserve		(14,584)	43,290
Accumulated loss		(265,918,628)	(164,188,892)
Total equity		<u>384,048,403</u>	<u>149,259,030</u>
Current liabilities			
Trade and other payables	6	551,287	381,838
Accrued liabilities	7	283,309	533,880
Current tax payable		(615,538)	207,491
Total liabilities		<u>219,058</u>	<u>1,123,209</u>
Total equity and liabilities		<u>384,267,461</u>	<u>150,382,239</u>

[Table of Contents](#)

Statement of profit or loss
For the year ended December 31, 2023

		Years ended December 31,	
		2023	2022
	Note	€	€
Share in results of participating interests	1, 9	(100,478,637)	(75,872,853)
Other loss and expenses after taxes		(396,431)	(459,704)
Loss for the year after tax		(100,875,068)	(76,332,557)

Notes to the Company financial statements

General

These company financial statements and the consolidated financial statements together constitute the statutory financial statements of Pharvaris N.V. (hereinafter: the “Company” or “Pharvaris”). The financial information of the Company is included in the Group’s consolidated financial statements, as presented on pages 120 to 140. The company’s financial statements are prepared based on the accounting principles of recognition, measurement and determination of profit, as applied in the consolidated financial statements.

On September 30, 2015, Pharvaris N.V. was incorporated and is based in Leiden, the Netherlands. The address of its registered office is Emmy Noetherweg 2, Leiden.

The description of the Company’s activities and the Group structure as included in the notes to the consolidated financial statements also apply to the company financial statements.

Accounting policies

The 2023 company financial statements including the notes thereon have been prepared in accordance with Part 9 of Book 2 of the Dutch Civil Code. Section 2:362 (8) of the Dutch Civil Code, allows companies that apply IFRS as issued by the European Union in their consolidated financial statements to use the same measurement principles in their company financial statements. Pharvaris has prepared these company financial statements using this provision. These principles also include the classification and presentation of financial instruments, being equity instruments or financial liabilities.

Since Pharvaris N.V.’s statement of profit or loss for 2023 is recognized in the consolidated financial statements, it is sufficient in the company financial statements to present a condensed statement of profit or loss in accordance with section 402 of Book 2 of the Dutch Civil Code.

Participating interest

Consolidated subsidiaries are all entities (including intermediate subsidiaries) over which the company has control. The Company controls an entity when it is exposed, or has rights, to variable returns from its involvement with the subsidiary and has the ability to affect those returns through its power over the subsidiary. Subsidiaries are recognised from the date on which control is transferred to the Company or its intermediate holding entities. They are derecognised from the date that control ceases.

Investments in subsidiaries are measured using the net asset value method. The measurement of the financial fixed assets under the net asset value method is based on the measurement principles of assets, provisions and liabilities, and the determination of profit as applied in the consolidated financial statements. When subsidiaries have an equity deficit they are measured at zero under the net asset value method, unless the Company has given a liability undertaking or any other guarantee for the consolidated group company. In case of the latter, the Company recognises a provision in the statement of financial position equal to the negative net asset value of the group company. The Company has direct and indirect interests in the subsidiaries listed in the Other Information section of the consolidated financial statements. The company applies the Dutch GAAP with respect to the presentation and disclosure requirements. Under Dutch GAAP the measurement principles applied in the separate financial statements are equal to those applied in the consolidated financial statements due to the fact participating interests and subsidiaries are measured based on the net asset value method (which have similar characteristics to the equity method under IFRS).

Share of result in participating interest

The share of result of participating interests consists of the share of the Group in the results of these participating interests.

Corporate income tax

The Company is the head of the fiscal unity including Pharvaris Holdings B.V. and Pharvaris Netherlands B.V. The Company recognizes the portion of corporate income tax charge that it would owe as an independent taxpayer, taking into account the allocation of the advantages of the fiscal unity. Deferred tax positions are recognized by the head of the fiscal unity in total. Under the standard conditions, the members of the tax group are jointly and severally liable for any corporate income taxes payable by the Company.

Presentation of company financial statements

The structure of the Company statement of financial position and Company Statement of profit or loss are aligned as much as possible with the Consolidated statements in order to achieve optimal transparency between the consolidated financial statements and the company financial statements. The Company statement of financial position has been prepared before the appropriation of results.

1. Financial fixed assets

Movements in the financial fixed assets were as follows:

	Investment in consolidated subsidiaries	Loans to consolidated subsidiaries	Total
	€	€	€
At January 1, 2023			
Net book value	3,135,051	131,548,189	134,683,240
Movements in book value			
Investments / (conversion into equity)	447,942,054	(120,247,622)	327,694,432
Exchange differences	(14,584)	(96,682)	(111,266)
Share of loss of participations	(100,478,637)	—	(100,478,637)
Other movements	—	(655,581)	(655,581)
	347,448,833	(120,999,886)	226,448,947
At December 31, 2023			
Net book value	<u>350,583,884</u>	<u>10,548,303</u>	<u>361,132,187</u>

Pharvaris Holdings B.V. reported a loss of €100,478,637 for the year ended December 31, 2023 (2022: €75,872,853). The receivable from consolidated subsidiaries is considered to be part of the investment in subsidiaries and the Company intends to convert these outstanding balances into equity. The fair value of the loans to subsidiaries approximates the carrying amount.

The investment in subsidiaries is carried at €361,132,187 on December 31, 2023 (2022: €134,683,240). The investment of €327,694,432 relates to capital contributions into a group company to satisfy the capital needs of the group company. The loans to consolidated subsidiaries are in a current account with group companies, which is directly claimable.

The Company directly holds 100% of the shares of Pharvaris Holdings B.V. (2022: 100%) and indirectly holds 100% of the shares of Pharvaris Netherlands B.V. (2022: 100%), 100% of the shares of Pharvaris Inc. (2022: 100%) and 100% of the shares of Pharvaris GmbH (2022: 100%) via Pharvaris Holdings B.V.

2. Receivables

	<u>December 31, 2023</u>	<u>December 31, 2022</u>
	€	€
VAT receivables	69,883	116,948
	<u>69,883</u>	<u>116,948</u>

The receivables do not bear any interest, the fair value approximates the book value. All receivables fall due within one year.

3. Prepayments, other receivables and deferred expenses

	December 31, 2023	December 31, 2022
	€	€
Prepayments	414,185	500,905
Other receivables and deferred expenses	447,310	524,486
	<u>861,495</u>	<u>1,025,391</u>

Prepayments per December 31, 2023 and 2022 mainly relate to prepaid D&O insurance. Other receivables and deferred expenses per December 31, 2023 mainly consist of deferred transaction costs related to Group's in-process equity financing (refer to note 13 in the consolidated financial statements). 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. The fair value of the prepayments, other receivables and deferred expenses approximates the carrying amount.

4. Cash and cash equivalents

	December 31, 2023	December 31, 2022
	€	€
Cash and cash equivalents	22,203,896	14,556,660
	<u>22,203,896</u>	<u>14,556,660</u>

The Cash and cash equivalents consist of bank balances and are not subject to any restriction.

5. Equity

On December 31, 2023, the Company's 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, 2023, the total number of issued and fully paid shares was 52,290,212 (2022: 33,816,459; 2021: 33,151,881). On December 31, 2023, the issued share capital totaled €6.3 million (2022: €4.1 million; 2021: €4.0 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.

Ordinary shares hold the right to one vote per share.

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.

	Share capital	Share premium	Other reserves	Legal 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)
Increase in par value	—	—	—	—	—	—
Issue of share capital	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	9,177	1,019,372	(954,157)	—	(287,934)	(213,542)
Share-based payments	—	—	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)
Increase in par value	—	—	—	—	—	—
Issue of share capital	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	46,998	3,243,359	(2,937,889)	—	(854,668)	(502,200)
Share-based payments	—	—	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

Legal reserve

As of December 31, 2023 the legal reserve amounted to (€14,584) (2022: €43,290) and relate to unrealized currency translation losses. Pursuant to Dutch law, limitations exist relating to the distribution of shareholder's equity for the entire amount of legal reserve. By their nature, unrealized losses relating to the currency translation differences reduce shareholders' equity and thereby distributable amounts.

[Table of Contents](#)

Appropriation of the result for 2023 and 2022

The result for the years 2023 and 2022 has been transferred to accumulated losses.

Difference in equity and loss between the company and consolidated financial statements

There is no difference between equity according to the company balance sheet and equity according to the consolidated balance sheet as well as the result according to the Company income statement and result according to the consolidated income statement for the year ended December 31, 2023 and 2022.

6. Trade and other payables

	<u>December 31, 2023</u>	<u>December 31, 2022</u>
	€	€
Trade payables	551,287	381,838
	<u>551,287</u>	<u>381,838</u>

Trade and other payables fall due within one year.

7. Accrued liabilities

	December 31, 2023	December 31, 2022
	€	€
Consulting and accounting fee accruals	283,309	533,880
	<u>283,309</u>	<u>533,880</u>

All the accrued liabilities are due within twelve months after year-end and qualify as short-term liabilities.

8. Commitments and contingencies

The Company had no contingent liabilities and no contingent assets at December 31, 2023 and 2022.

Fiscal unity

The Company is the head of the fiscal unity Pharvaris N.V. in the Netherlands for income taxes and is jointly and severally liable for the income tax liabilities of the fiscal unity. Reference is made to note 10 of these financial statements.

9. Share in results of participating interests

This represents the share of the Company in the results of its participating interest of Pharvaris Holdings B.V. Reference is made to Note 1 of these financial statements.

[Table of Contents](#)

10. Income taxes

Pharvaris N.V. forms a corporate income tax group, fiscal unity, with Pharvaris Netherlands B.V. and Pharvaris Holdings B.V. As head of the fiscal unity, the company financial statements of Pharvaris N.V. recognise the entire tax position of the fiscal unity.

The current tax expenses of €714,733 for the year ended December 31, 2023 relates to the result of a cost-plus agreement between the Dutch entities and the Group's principal entity in Switzerland resulting in a taxable profit in the Netherlands. This is fully offset by the deferred tax benefit of €714,733 for the year ended December 31, 2023 which is directly recognized in equity and relates to the deferred tax effect of share issuance costs accounted for in share premium but which are tax deductible. For the year ended December 31, 2022, a tax benefit of €257,734 was directly recognized in equity.

The Company did not recognize the tax benefit of the losses incurred in previous years. The fiscal unity has tax loss carry-forwards of approximately €30.7 million (2022: €14.9 million), that are available for offsetting against future taxable profits of the companies in which the losses arose.

Tax loss carry-forwards incurred in current and prior years will expire as follows:

Year	Tax losses € million
Unlimited	30.7
Total carry-forward losses	30.7

Deferred tax

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 statement of profit or loss. 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.

	R&D expenses	Other Receivables	Total
	€	€	€
Deferred tax assets			
At January 1, 2022	1,909,917	—	1,909,917
(Charged)/credited			
- Profit or loss	(117,533)	—	(117,533)
- Currency translation differences	—	—	—
At December 31, 2022	1,792,384	—	1,792,384
Deferred tax liability			
At January 1, 2022	—	(1,909,917)	(1,909,917)
(Charged)/credited			
- Profit or loss	—	117,533	117,533
- Currency translation differences	—	—	—
At December 31, 2022	—	(1,792,384)	(1,792,384)
Net deferred tax assets at December 31, 2022			—

	R&D expenses	Other Receivables	Total
	€	€	€
Deferred tax assets			
At January 1, 2023	1,792,384	—	1,792,384
(Charged)/credited			
- Profit or loss	(37,609)	—	(37,609)
- Currency translation differences	—	—	—
At December 31, 2023	1,754,775	—	1,754,775
Deferred tax liability			
At January 1, 2023	—	(1,792,384)	(1,792,384)
(Charged)/credited			
- Profit or loss	—	37,609	37,609
- Currency translation differences	—	—	—
At December 31, 2023	—	(1,754,775)	(1,754,775)
Net deferred tax assets at December 31, 2023			—

[Table of Contents](#)

The total unrecognized deferred tax assets from temporary differences amounts to €9.3 million (2022: €5.3 million). No deferred tax balances in relation to investments in subsidiaries, associates and interests in joint arrangements are considered, due to the fact that the timing of the reversal of the temporary differences can be controlled by the Company and it is probable that the temporary differences will not reverse in the foreseeable future.

11. Related parties

Note 1.2 of the consolidated financial statements provides information about the Group's structure, including details of the subsidiaries and the holding company and the total amount of transactions that have been entered into with related parties for the relevant financial year. Reference is made to Note 20 of the consolidated financial statements.

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, 2022 and 2021, payments to Charité CRO with respect to this service contract amounted to €0.5 million, €0.4 million and €608, respectively.

12. Remuneration of the board of Directors and Key management

The emoluments, including pension costs as referred to in Section 2:383(1) of the Netherlands Civil Code, charged in the financial year to the Company and group companies by the Board of Directors members amounts to €3,760,144 (2022: €5,997,126).

The below table shows the remuneration of the individual members of the Board of Directors for the year ended December 31, 2023 and 2022 in euro:

	Salary	Bonus	Pension and social securities	Management fee	Share-based compensation	Total remuneration 2023	Total remuneration 2022
	€	€	€	€	€	€	€
Mr. B. Modig	595,693	265,760	73,831	-	1,401,365	2,336,649	2,413,678
Mr. H. Schikan	-	-	-	56,450	139,404	195,854	269,146
Mr. D. Meeker	-	-	-	87,136	373,431	460,567	281,888
Mr. R. Glassman	-	-	-	45,072	198,914	243,986	195,605
Ms. V. Monges	-	-	-	57,106	201,729	258,835	309,621
Ms. E. Björk	-	-	-	41,591	255,859	297,450	318,576
Ms. A. de Jonge - Schuermans(1)	-	-	-	27,610	(60,807)	(33,197)	236,603

(1) Not part of the Board of Directors per year end 2023.

Mr. Modig has received a bonus on the realization of targets set by the Group.

Share-based compensation represents the impact in the result of the Company for the expenses granted to the members of the Board of Directors.

The Key management of the Group is paid through the group companies, no costs related to Key management are included in the company financial statements. Further reference is made to note 20 of the consolidated financial statements.

13. Employee benefits and information

The Company had no employees during the fiscal year 2023 (2022: nil).

The Company is responsible for settling share-based payment transactions with employees of its subsidiaries, and these are recognized as equity-settled share-based payment transactions since they are settled in shares of the Company. Total costs related to share-based payments for €10,663,226 (2022: €11,349,200) are included in "Share in results of participating interests" in the company financial statements, with a corresponding adjustment to equity. Reference is made to note 18 in the consolidated financial statements for disclosure on the share-based payments.

[Table of Contents](#)

14. Independent Auditor's fee

	2023	2022
	€	€
Audit of financial statements	343,500	319,000
Other assurance services	541,247	492,876
	<u>884,747</u>	<u>811,876</u>

Other assurance services relate mainly to quarterly reviews of financial statements of the Company and assurance of US comfort letters in connection with F-3 / ATM program.

15. Events after the reporting period

On April 10, 2024, the Company announced the appointment of Mr. David W. Nassif to the newly created position of Chief Financial Officer, effective April 15, 2024. As Chief Financial Officer, Mr. Nassif will lead and oversee all of the Company's financial activities and will be responsible for maintaining the financial health of the Company.

Joan Schmidt, our Chief Legal Officer, has announced that she will be leaving the Company effective June 1, 2024. David Nassif will assume oversight of the legal and compliance department and will act as the corporate secretary until a successor joins the Company.

[Table of Contents](#)

Signatories to the financial statements

Leiden, May 30, 2024

Pharvaris N.V.
Board of directors

/s/ D. Meeker

D. Meeker

/s/ E. Björk

E. Björk

/s/ V. Monges

V. Monges

/s/ R. Glassman

R. Glassman

/s/ B.A.E. Modig

B.A.E. Modig

/s/ J.G.C.P. Schikan

J.G.C.P. Schikan

Other Information

Independent auditor's report

The independent auditor's report is included in the next page

Profit appropriation provisions

Pursuant to the Company's article 30 of the articles of association, any profits shown in the adopted statutory annual accounts of the Company shall be appropriated as follows, and in the following order of priority:

1. the Board shall determine which part of the profits shall be added to the Company's reserves; and
2. subject to a proposal by the Board to that effect, the remaining profits shall be at the disposal of the General Meeting for distribution on the shares.

Shares carrying limited economic entitlement

There are currently no outstanding shares which carry a limited entitlement to the profits or reserves in the Company.

Branches

The Company has no branch offices.

Signature page to the Dutch Annual Report of Pharvaris N.V. for the fiscal year ended December 31, 2023



Independent auditor's report

To: the general meeting and the of Pharvaris N.V.

Report on the audit of the financial statements 2023

Our opinion

In our opinion:

- the consolidated financial statements of Pharvaris N.V. together with its subsidiaries ('the Group') give a true and fair view of the financial position of the Group as at 31 December 2023 and of its result and cash flows for the year then ended in accordance with International Financial Reporting Standards as adopted in the European Union ('EU-IFRS') and with Part 9 of Book 2 of the Dutch Civil Code;
- the company financial statements of Pharvaris N.V. ('the Company') give a true and fair view of the financial position of the Company as at 31 December 2023 and of its result for the year then ended in accordance with Part 9 of Book 2 of the Dutch Civil Code.

What we have audited

We have audited the accompanying financial statements 2023 of Pharvaris N.V., Leiden. The financial statements comprise the consolidated financial statements of the Group and the company financial statements.

The consolidated financial statements comprise:

- the consolidated statement of financial position as at 31 December 2023;
- the following statements for 2023: the consolidated statement of loss and comprehensive loss, the consolidated statement of changes in shareholders' equity, and the consolidated statement of cash flows; and
- the notes to the consolidated financial statements, including material accounting policy information and other explanatory information.

The company financial statements comprise:

- the statement of financial position as at 31 December 2023;
- the statement of profit or loss for the year then ended; and
- the notes to the company financial statements, comprising a summary of the accounting policies applied and other explanatory information.

The financial reporting framework applied in the preparation of the financial statements is EU-IFRS and the relevant provisions of Part 9 of Book 2 of the Dutch Civil Code for the consolidated financial statements and Part 9 of Book 2 of the Dutch Civil Code for the company financial statements.

NLE00023836.1.1

PricewaterhouseCoopers Accountants N.V., Thomas R. Malthusstraat 5, 1066 JR Amsterdam, P.O. Box 90357, 1006 BJ Amsterdam, the Netherlands

T: +31 (0) 88 792 00 20, F: +31 (0) 88 792 96 40, www.pwc.nl

'PwC' is the brand under which PricewaterhouseCoopers Accountants N.V. (Chamber of Commerce 34180285), PricewaterhouseCoopers Belastingadviseurs N.V. (Chamber of Commerce 34180284), PricewaterhouseCoopers Advisory N.V. (Chamber of Commerce 34180287), PricewaterhouseCoopers Compliance Services B.V. (Chamber of Commerce 51414406), PricewaterhouseCoopers Pensions, Actuarial & Insurance Services B.V. (Chamber of Commerce 54226368), PricewaterhouseCoopers B.V. (Chamber of Commerce 34180289) and other companies operate and provide services. These services are governed by General Terms and Conditions ('algemene voorwaarden'), which include provisions regarding our liability. Purchases by these companies are governed by General Terms and Conditions of Purchase ('algemene inkoopvoorwaarden'). At www.pwc.nl more detailed information on these companies is available, including these General Terms and Conditions and the General Terms and Conditions of Purchase, which have also been filed at the Amsterdam Chamber of Commerce.



The basis for our opinion

We conducted our audit in accordance with Dutch law, including the Dutch Standards on Auditing. We have further described our responsibilities under those standards in the section 'Our responsibilities for the audit of the financial statements' of our report.

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

Independence

We are independent of Pharvaris N.V. in accordance with the 'Wet toezicht accountantsorganisaties' (Wta, Audit firms supervision act), the 'Verordening inzake de onafhankelijkheid van accountants bij assuranceopdrachten' (ViO, Code of Ethics for Professional Accountants, a regulation with respect to independence) and other relevant independence regulations in the Netherlands. Furthermore, we have complied with the 'Verordening gedrags- en beroepsregels accountants' (VGBA, Dutch Code of Ethics).

Our audit approach

We designed our audit procedures, including our procedures with respect to the key audit matters, fraud and going concern, and the matters resulting from that, in the context of our audit of the financial statements as a whole and in forming our opinion thereon. The information in support of our opinion, such as our findings and observations related to individual key audit matters, the audit approach fraud risk and the audit approach going concern was addressed in this context, and we do not provide separate opinions or conclusions on these matters.

Overview and context

Pharvaris N.V. is a clinical-stage biopharmaceutical company, currently focussing on the development and commercialisation of angioedema and other bradykinin-mediated diseases. Pharvaris N.V. was incorporated on 30 September 2015 and is headquartered in Leiden, the Netherlands. It is the parent company of a group of entities, whose financial information is also included in the consolidated financial statements.

As part of designing our audit, we determined materiality and assessed the risks of material misstatement in the financial statements. In particular, we considered where the management made important judgements, for example, in respect of significant accounting estimates that involved making assumptions and considering future events that are inherently uncertain.

In note 2.19 of the consolidated financial statements, the Company describes the areas of judgement in applying accounting policies and the key sources of estimation uncertainty. Given the significant judgments made by management in developing the estimate for establishing research and development accruals and as a result of the higher degree of effort in auditing these accruals, we considered this to be a key audit matter as set out in the section 'Key audit matters' of this report.

Other areas of focus, that were not considered as key audit matters, were the accounting and disclosure related to share-based payments and the accounting for deferred taxes.

As in all our audits, we also addressed the risk of management override of controls, including evaluating whether there was evidence of bias by management that may represent a risk of material misstatement due to fraud.

We ensured that the audit team included the appropriate skills and competences, which are needed for the audit of a clinical stage biopharmaceutical company. We therefore included experts and specialists in the area of share-based payments in our team.

The outline of our audit approach was as follows:



Materiality

The scope of our audit was influenced by the application of materiality, which is further explained in the section ‘Our responsibilities for the audit of the financial statements’.

Based on our professional judgement we determined certain quantitative thresholds for materiality, including the overall materiality for the financial statements as a whole as set out in the table below. These, together with qualitative considerations, helped us to determine the nature, timing and extent of our audit procedures on the individual financial statement line items and disclosures and to evaluate the effect of identified misstatements, both individually and in aggregate, on the financial statements as a whole and on our opinion.

Overall group materiality	€4,900,000 (2022: €867,000).
Basis for determining materiality	We used our professional judgement to determine overall materiality. As a basis for our judgement, we used 5% of ‘loss before tax’.
Rationale for benchmark applied	We used ‘loss before tax’ as the primary benchmark, a generally accepted auditing practice, based on our analysis of the common information needs of the users of the financial statements and to align with the industry practice. On this basis, we believe that loss before tax is the most relevant metric for the financial performance of the Company.



We also take misstatements and/or possible misstatements into account that, in our judgement, are material for qualitative reasons.

We agreed with the board of directors that we would report to them any misstatement identified during our audit above €245,000 (2022: €43,000) as well as misstatements below that amount that, in our view, warranted reporting for qualitative reasons.

The scope of our group audit

We tailored the scope of our audit to ensure that we, in aggregate, provide sufficient coverage of the financial statements for us to be able to give an opinion on the financial statements as a whole, taking into account the management structure of the Group, the nature of operations of its components, the accounting processes and controls, and the markets in which the components of the Group operate. In establishing the overall group audit strategy and plan, we determined that we, as the group engagement team, will perform all the audit procedures for the audit of the Group and company financial statements as the financial reporting and accounting functions for all entities in the Group are located, operated, and managed centrally in Leiden.

In total, in performing these procedures, we achieved the following coverage on the financial line items:

Revenue	100%
Total assets	100%
Profit before tax	100%

By performing the procedures outlined above, we have been able to obtain sufficient and appropriate audit evidence on the Group's financial information, to provide a basis for our opinion on the financial statements.

Audit approach fraud risks

We identified and assessed the risks of material misstatements of the financial statements due to fraud. During our audit we obtained an understanding of Pharvaris N.V. and its environment and the components of the internal control system. This included the management's risk assessment process, the management's process for responding to the risks of fraud and monitoring the internal control system and how the board of directors exercised oversight, as well as the outcomes. We note that the management has not formalised its fraud risk assessment.

We evaluated the design and relevant aspects of the internal control system with respect to the risks of material misstatements due to fraud and in particular the fraud risk assessment, as well as the code of conduct and whistleblower procedures.

We asked members of the management team as well as the human resources department, legal and compliance department and the board of directors whether they are aware of any actual or suspected fraud. This did not result in signals of actual or suspected fraud that may lead to a material misstatement.



As part of our process of identifying fraud risks, we evaluated fraud risk factors with respect to financial reporting fraud, misappropriation of assets and bribery and corruption. We evaluated whether these factors indicate that a risk of material misstatement due to fraud is present.

<i>Identified fraud risks</i>	<i>Our audit work and observations</i>
<p><i>Risk of management override of controls</i> Management is in a unique position to perpetrate fraud because of management's ability to manipulate accounting records and prepare fraudulent financial statements by overriding controls that otherwise appear to be operating effectively.</p> <p>We paid attention to the risk of management override of controls including risks of potential misstatements due to fraud based on an analysis of potential interests of management in areas where management would most likely override controls, i.e., accounting for significant unusual transactions, recording of critical accounting estimates, booking of manual journal entries, or via incomplete/inaccurate disclosures.</p>	<p>We evaluated the design and implementation of the internal control system in the processes of generating and processing journal entries and making estimates.</p> <p>We selected journal entries based on risk criteria and conducted specific audit procedures for these entries. These procedures include, among others, inspection of the entries to source documentation.</p> <p>We also performed specific audit procedures related to important estimates of management as disclosed in Note 2.19 to the financial statements. We specifically paid attention to the inherent risk of bias of management in estimates and existence of any significant transactions outside the normal course of business.</p> <p>Our audit procedures did not lead to specific indications of fraud or suspicions of fraud with respect to management override of controls.</p>
<p><i>Risk of unauthorised/fraudulent payments</i> As disclosed in note 4.2 of the annual report, due to the existence material weaknesses identified in prior year's audit, which have remained unremediated as of 31 December 2023, we identified the risk of unauthorised/fraudulent payments as a fraud risk.</p>	<p>We evaluated the design and implementation of the internal control system in the purchase and payables business process.</p> <p>We performed testing of payments on a sample basis throughout the year to ensure validity and authorisation of the payments.</p> <p>We verified the existence of vendors and appropriateness of payments to these vendors by tracing the vendor information to vendor invoices, external sources, contracts, prior year knowledge etc.</p> <p>We evaluated the business rationale for the selected payment transactions and ensured that they were incurred in the normal course of business.</p> <p>Our audit procedures did not lead to specific indications of fraud or suspicions of fraud with respect to payments.</p>

We incorporated an element of unpredictability in our audit. We reviewed lawyer's letters and correspondence with regulators. During the audit, we remained alert to indications of fraud. Furthermore, we considered the outcome of our other audit procedures and evaluated whether any findings were indicative of fraud or non-compliance with laws and regulations.



Audit approach going concern

The board of directors prepared the financial statements on the assumption that the Company is a going concern and that it will continue all its operations for at least twelve months from the date of preparation of the financial statements.

Our procedures to evaluate the management's going-concern assessment included, among others:

- considering whether the management identified events or conditions that may cast significant doubt on the Company's ability to continue as a going concern (hereafter: going-concern risks);
- considering whether the management's going-concern assessment includes all relevant information of which we are aware as a result of our audit by review of the minutes of meetings of the board of directors and inquiring with the management regarding the most important assumptions underlying their going-concern assessment;
- evaluating the management's current budget including cash flows for at least twelve months from the date of preparation of the financial statements taken into account current developments and all relevant information of which we were aware as a result of our audit;
- obtaining independent external confirmations for the cash balance as at 31 December 2023; and
- performing inquiries of the management as to its knowledge of going-concern risks beyond the period of assessment.

Our procedures did not result in outcomes contrary to management's assumptions, judgements used, and disclosures made note 2,2 of the consolidated financial statements in the application of the going-concern assumption.

Key audit matters

Key audit matters are those matters that, in our professional judgement, were of most significance in the audit of the financial statements. We have communicated the key audit matters to the board of directors and the audit committee. The key audit matters are not a comprehensive reflection of all matters identified by our audit and that we discussed. In this section, we described the key audit matters and included a summary of the audit procedures we performed on those matters.

Considering the nature of the Group's business activities as well as the industry in which it operates, we consider the research and development accruals as a key audit matter for the current year. We have removed the key audit matter share-based payments that was reported in prior year.



This reflects the reduced level of judgement and associated audit risk and level of audit effort.

Key audit matter	Our audit work and observations
<p>Research and development accruals <i>Note 16 – consolidated financial statements.</i></p> <p>As described in Note 16 to the financial statements, the Company has recorded € 1.8 million and € 2.1 million in respect of clinical accrued liabilities and manufacturing accrued liabilities respectively for the estimated costs incurred but not yet billed or paid as of 31 December 2023. The Company makes estimates of accrued research and development expenses, including clinical trials and manufacturing, resulting from obligations under contracts with clinical research organisations ('CROs'), manufacturers, vendors and consultants. The financial terms of these contracts vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts.</p> <p>We identified the determination of aforementioned accruals as a key audit matter due to the application of significant management judgment over the estimate of services provided as of year-end. We also specifically consider that the amount of such accruals and related expenses recognised are sensitive to the estimate of the progress of the clinical trial.</p>	<p>The procedures we performed to address this key audit matter included:</p> <ul style="list-style-type: none">• We reviewed the Company's contractual agreements with respective clinical research organisations and any related changes to them in order to assess the impact to the amounts recorded including changes in scope and timing.• We obtained audit evidence regarding the research and development accruals and performed substantive testing procedures on the balance as at 31 December 2023. These procedures included:<ul style="list-style-type: none">i) evaluating amongst other things management's process for estimating accrued contracted research and development costs;ii) testing the completeness and accuracy of the data used to develop the estimate;iii) evaluating the reasonableness of the estimated costs incurred for the services which have not been invoiced by tracing (on sample basis) to underlying supporting documentation, such as underlying contracts, purchase orders and information received from certain clinical research organisations, where applicable.• We reviewed the disclosures in note 16 to the consolidated financial statements and deemed the disclosures in line with the requirements of applicable financial reporting framework. <p>We did not have any material findings based on the audit work performed and the audit evidence obtained.</p>

Report on the other information included in the annual report

The annual report contains other information. This includes all information in the annual report in addition to the financial statements and our auditor's report thereon.

Based on the procedures performed as set out below, we conclude that the other information:

- is consistent with the financial statements and does not contain material misstatements; and
- contains all the information regarding the directors' report and the other information that is required by Part 9 of Book 2 of the Dutch Civil Code.

We have read the other information. Based on our knowledge and the understanding obtained in our audit of the financial statements or otherwise, we have considered whether the other information contains material misstatements.



By performing our procedures, we comply with the requirements of Part 9 of Book 2 of the Dutch Civil Code and the Dutch Standard 720. The scope of such procedures was substantially less than the scope of those procedures performed in our audit of the financial statements.

The board of directors is responsible for the preparation of the other information, including the directors' report and the other information in accordance with Part 9 of Book 2 of the Dutch Civil Code.

Report on other legal and regulatory requirements

Our appointment

We were appointed as auditors of Pharvaris N.V. on 2 June 2020. This followed the passing of a resolution by the shareholders at the annual general meeting held on 23 June 2023. Our appointment has been renewed annually by shareholders and now represents a total period of uninterrupted engagement of four years.

Responsibilities for the financial statements and the audit

Responsibilities of the board of directors

The board of directors is responsible for:

- the preparation and fair presentation of the financial statements in accordance with EU-IFRS and Part 9 of Book 2 of the Dutch Civil Code; and for
- such internal control as the board of directors determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the board of directors is responsible for assessing the Company's ability to continue as a going concern. Based on the financial reporting frameworks mentioned, the board of directors should prepare the financial statements using the going-concern basis of accounting unless the board of directors either intends to liquidate the Company or to cease operations or has no realistic alternative but to do so. The board of directors should disclose in the financial statements any event and circumstances that may cast significant doubt on the Company's ability to continue as a going concern.

Our responsibilities for the audit of the financial statements

Our responsibility is to plan and perform an audit engagement in a manner that allows us to obtain sufficient and appropriate audit evidence to provide a basis for our opinion. Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error and to issue an auditor's report that includes our opinion. Reasonable assurance is a high but not absolute level of assurance, and is not a guarantee that an audit conducted in accordance with the Dutch Standards on Auditing will always detect a material misstatement when it exists. Misstatements may arise due to fraud or error. They are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

Materiality affects the nature, timing and extent of our audit procedures and the evaluation of the effect of identified misstatements on our opinion.



A more detailed description of our responsibilities is set out in the appendix to our report.

Amsterdam, 30 May 2024
PricewaterhouseCoopers Accountants N.V.

Original has been signed by W. Voorthuijsen RA

Appendix to our auditor's report on the financial statements 2023 of Pharvaris N.V.

In addition to what is included in our auditor's report, we have further set out in this appendix our responsibilities for the audit of the financial statements and explained what an audit involves.

The auditor's responsibilities for the audit of the financial statements

We have exercised professional judgement and have maintained professional scepticism throughout the audit in accordance with Dutch Standards on Auditing, ethical requirements and independence requirements. Our audit consisted, among other things of the following:

- Identifying and assessing the risks of material misstatement of the financial statements, whether due to fraud or error, designing and performing audit procedures responsive to those risks, and obtaining audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the intentional override of internal control.
- Obtaining an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control.
- Evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by the management.
- Concluding on the appropriateness of management's use of the going-concern basis of accounting, and based on the audit evidence obtained, concluding whether a material uncertainty exists related to events and/or conditions that may cast significant doubt on the Company's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report and are made in the context of our opinion on the financial statements as a whole. However, future events or conditions may cause the Company to cease to continue as a going concern.
- Evaluating the overall presentation, structure and content of the financial statements, including the disclosures, and evaluating whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation.

Considering our ultimate responsibility for the opinion on the consolidated financial statements, we are responsible for the direction, supervision and performance of the group audit. In this context, we have determined the nature and extent of the audit procedures for components of the Group to ensure that we performed enough work to be able to give an opinion on the financial statements as a whole. Determining factors are the geographic structure of the Group, the significance and/or risk profile of group entities or activities, the accounting processes and controls, and the industry in which the Group operates. On this basis, we selected group entities for which an audit or review of financial information or specific balances was considered necessary.

We communicate with the board of directors regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.



We provide the board of directors with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, related actions taken to eliminate threats or safeguards applied.

From the matters communicated with the board of directors, we determine those matters that were of most significance in the audit of the financial statements of the current period and are therefore the key audit matters. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, we determine that a matter should not be communicated in our report because the adverse consequences of doing so would reasonably be expected to outweigh the public interest benefits of such communication.